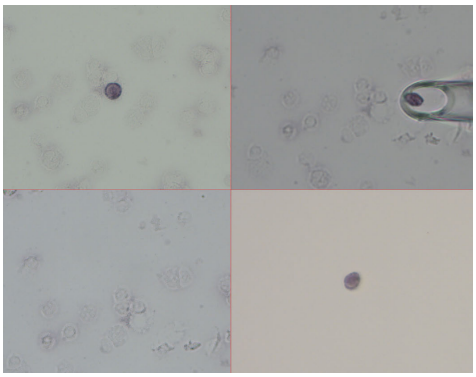
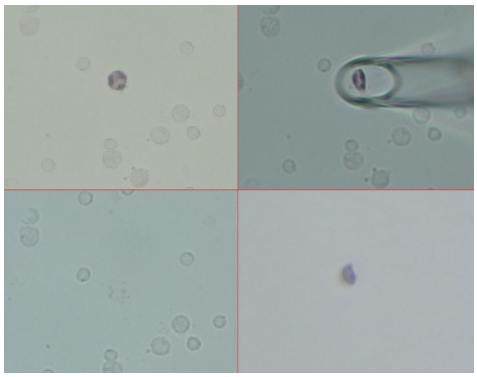
Figure S1: Isolation of disseminated tumor cells from bone marrow aspirates. Single cells isolated from patient MicMa003 (A), MicMa017 (B), MicMa019 (C), MicMa044 (D), MicMa083 (E), MicMa107 at diagnosis (F), and MicMa107 3 years post-diagnosis (G). Each panel documents the isolation process of the indicated single cell in four subsequent images taken before picking (top left), during micromanipulation (top right), of the area where the cell was picked from after micromanipulation (bottom left), and of the isolated cell in the lid (bottom right). The immunomorphological class of each cell is provided next to its name. Boxed names indicate control cells stained with an isotype control antibody.

A

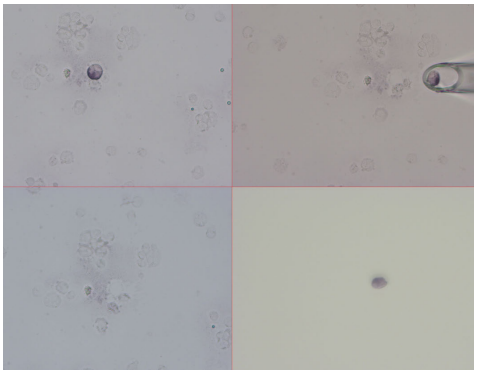
003A - TC



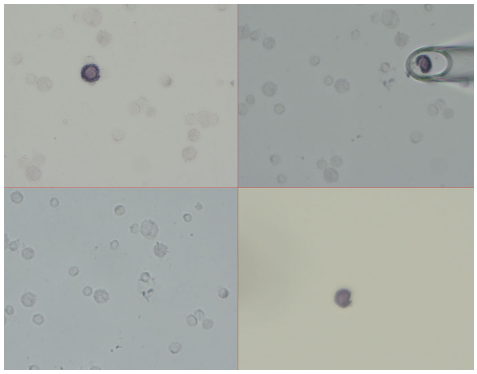
003B - TC



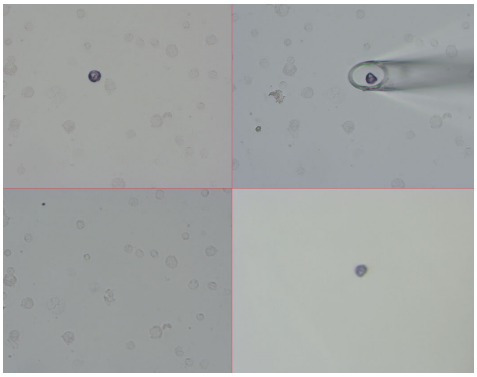
003C - TC



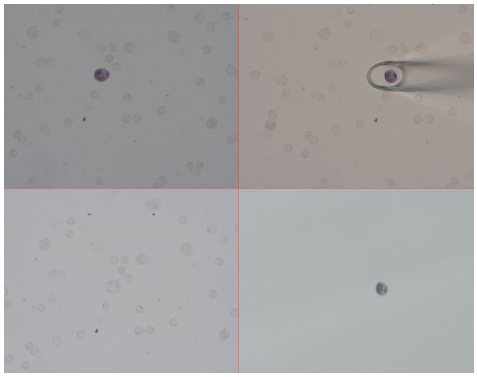
003D - TC



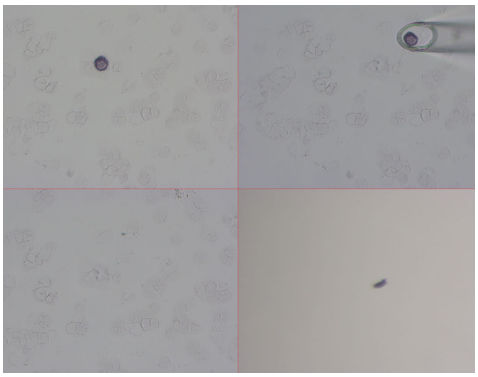
003E - TC



003F - PHC

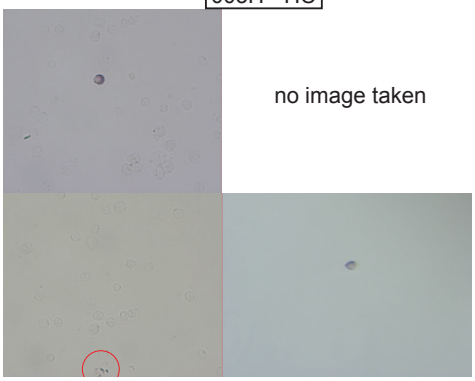


003G - PHC

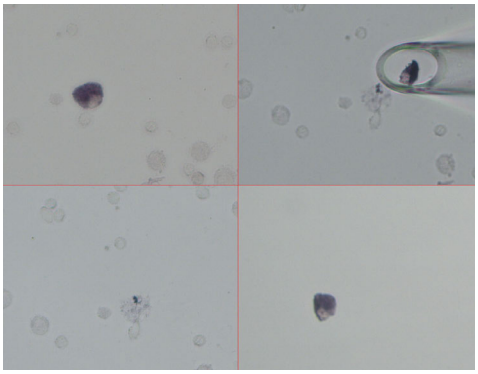


003H - HC

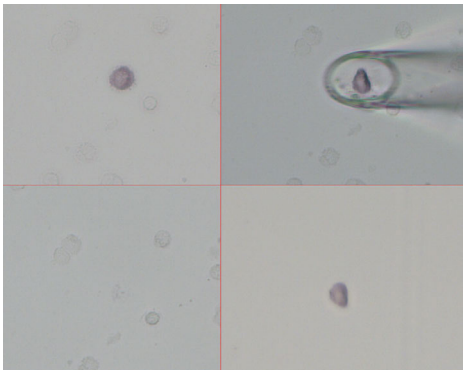
no image taken



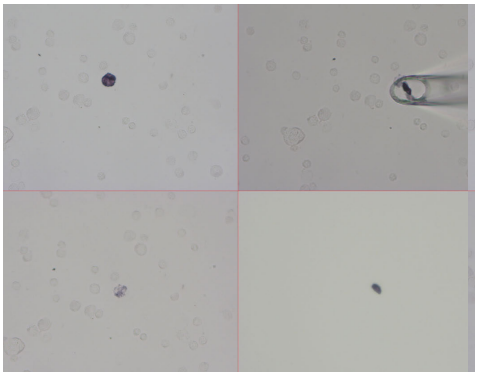
003I - HC



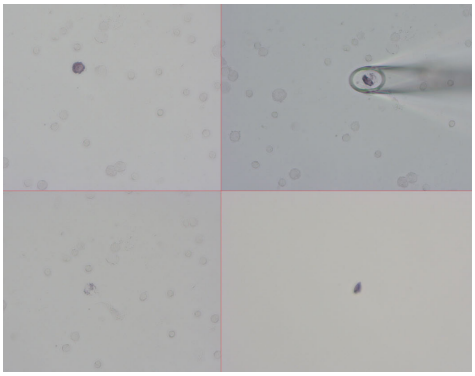
003J - uncertain



003K - uncertain

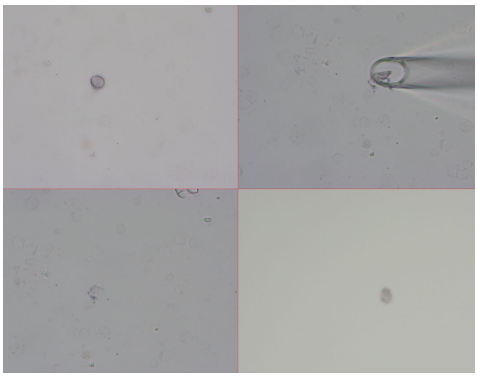


003L - PHC

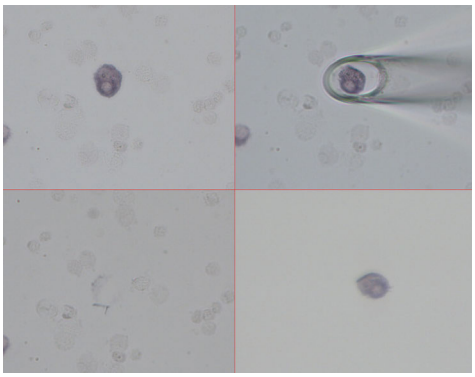


B

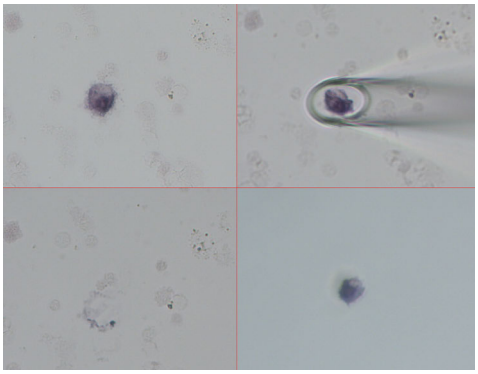
017A - uncertain



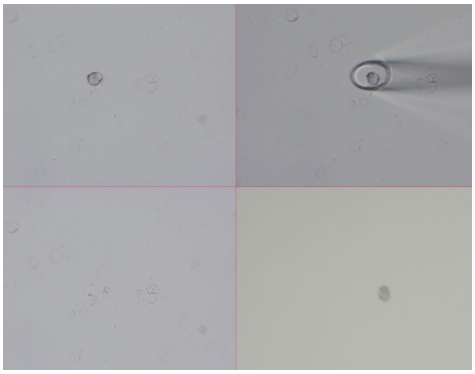
017B - uncertain



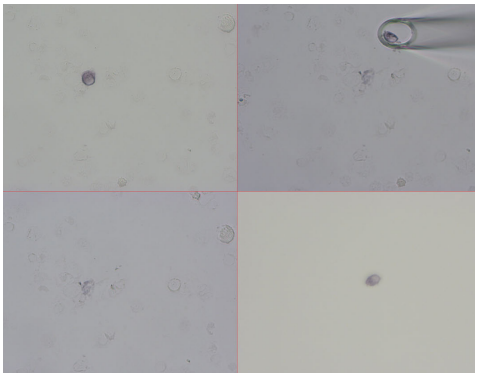
017C - uncertain



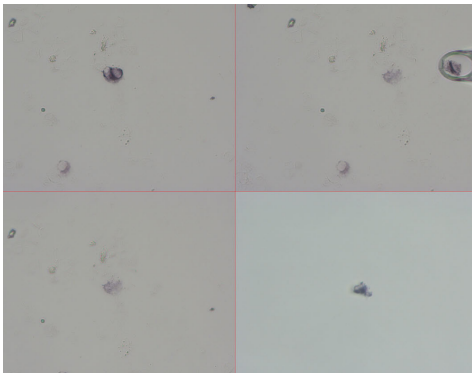
017D - uncertain



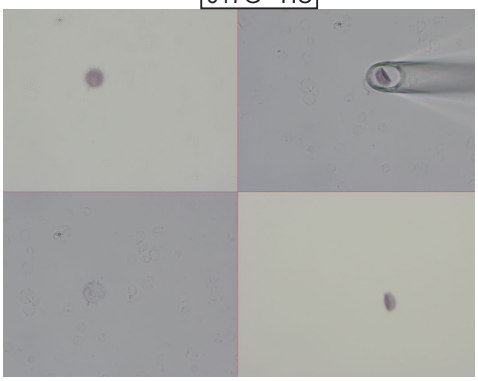
017E - PHC



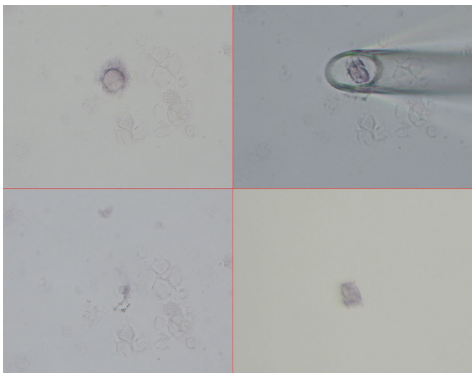
017F - uncertain



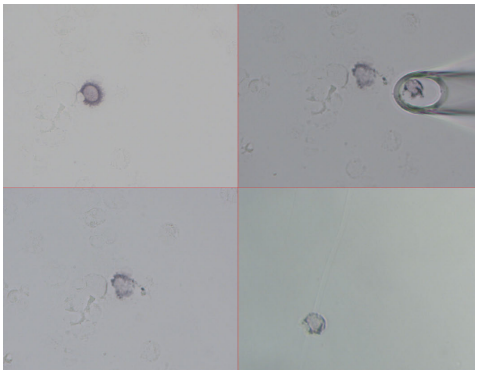
017G - HC



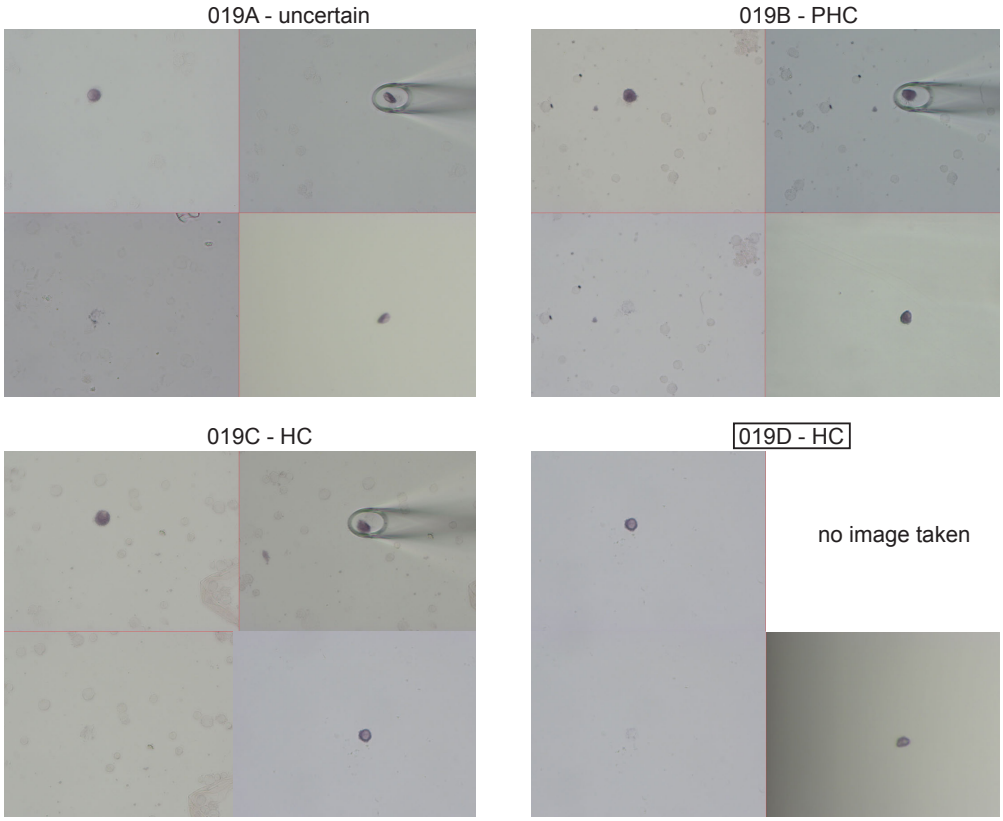
017H - PHC



017I - PHC

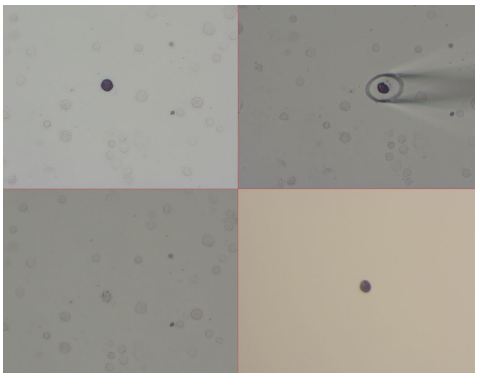


C

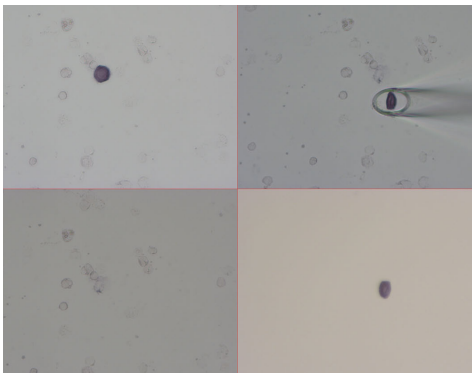


D

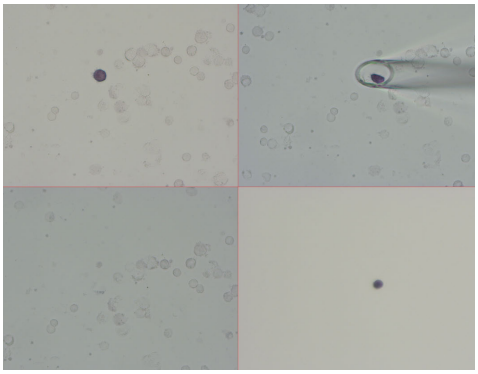
044A - TC



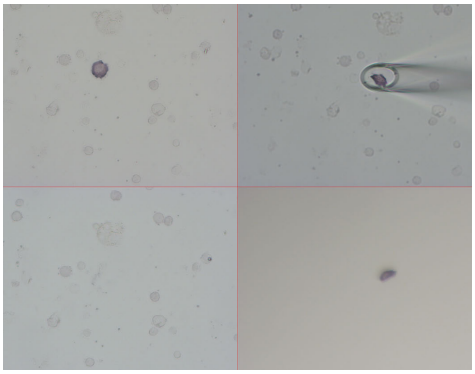
044B - TC



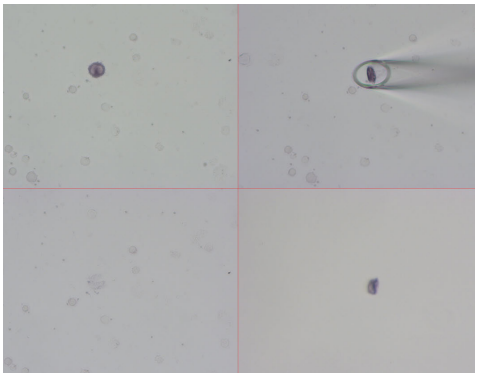
044C - uncertain



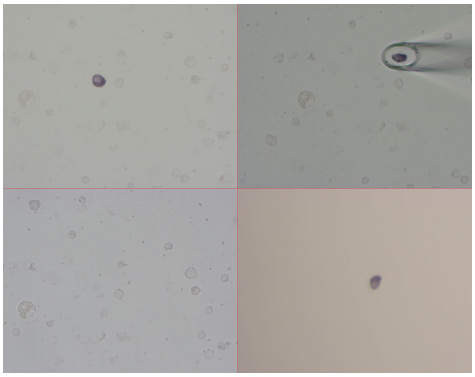
044D - PHC



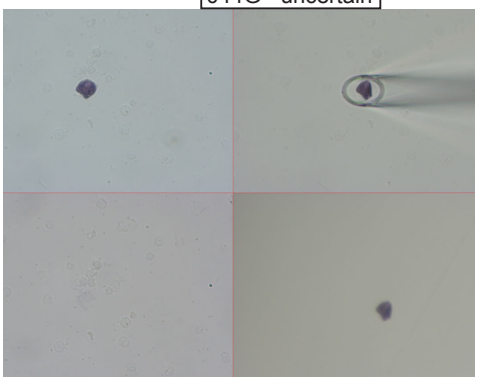
044E - TC



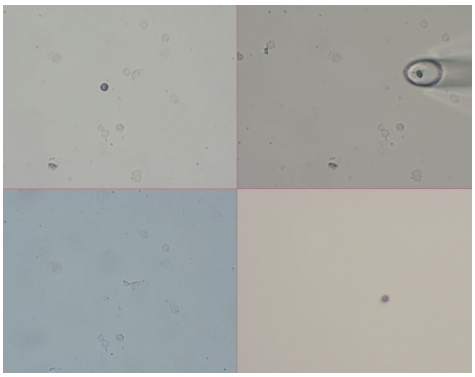
044F - PHC



044G - uncertain

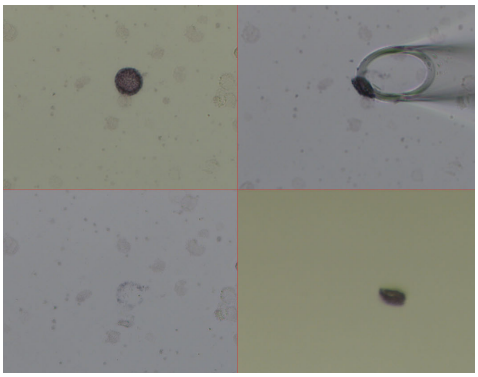


044H - PHC

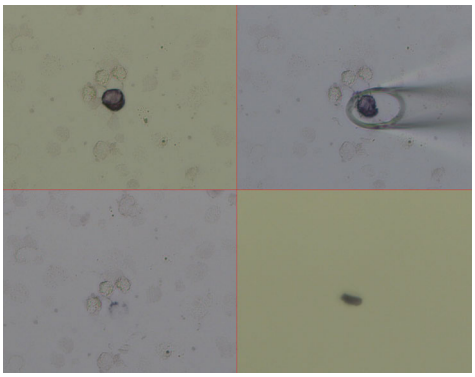


E

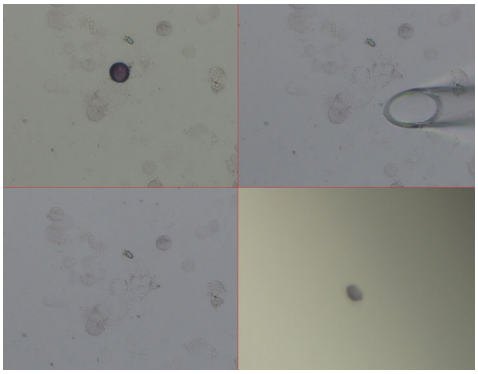
083A - TC



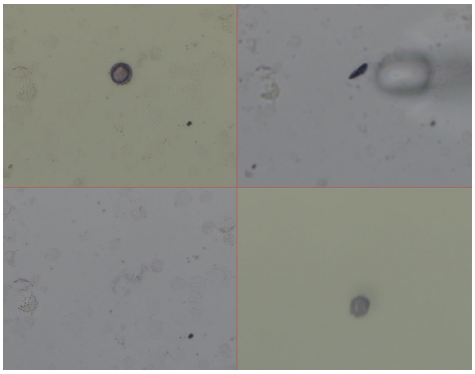
083B - TC



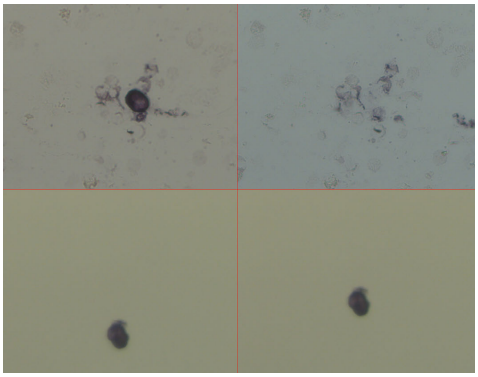
083C - TC



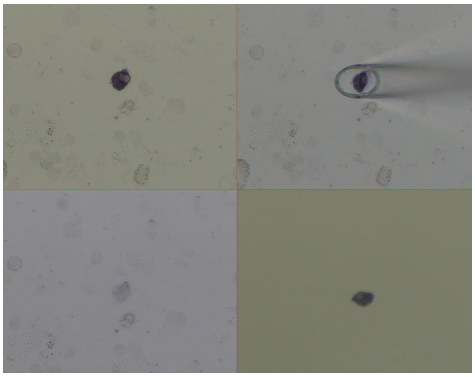
083D - TC



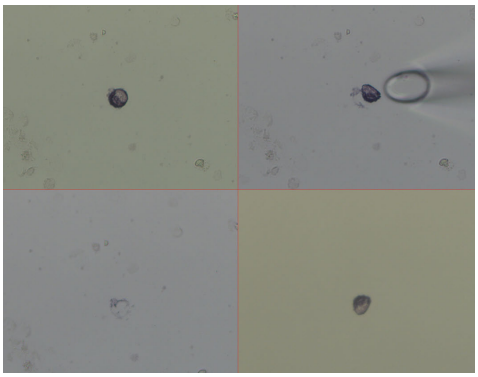
083E - TC



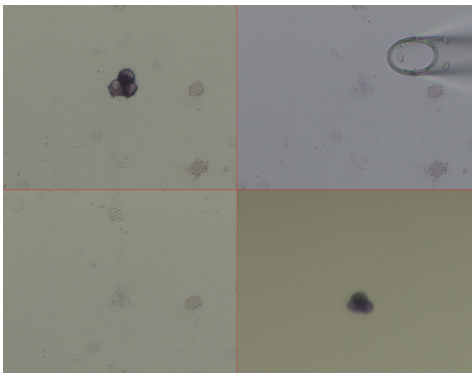
083F - PHC



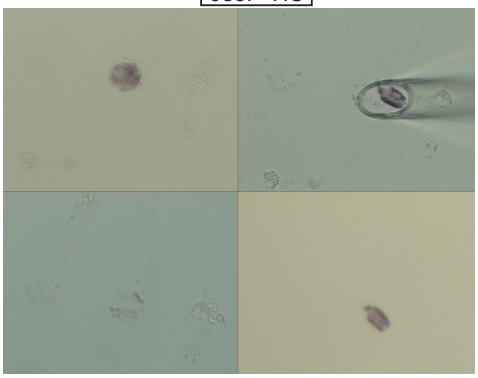
083G - TC



083H - TC

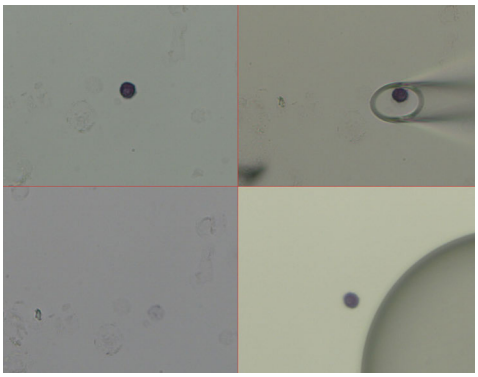


083I - HC

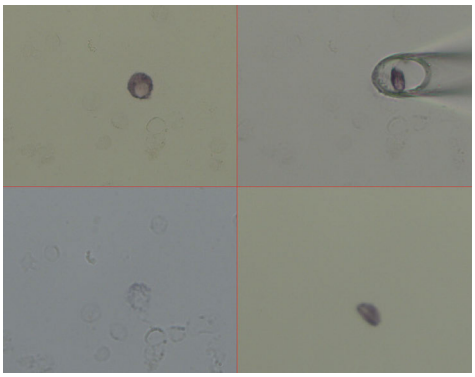


F

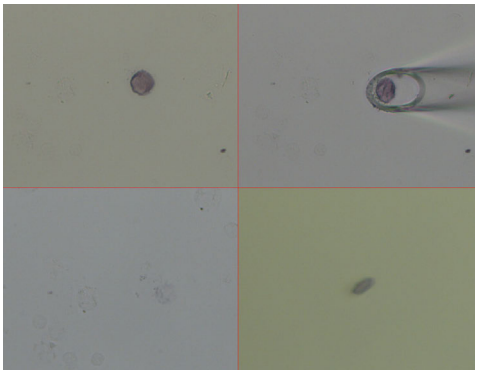
107A - TC



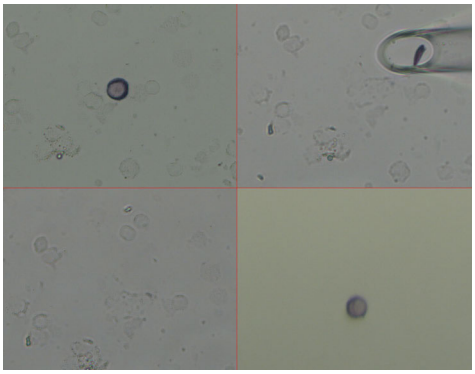
107B - uncertain



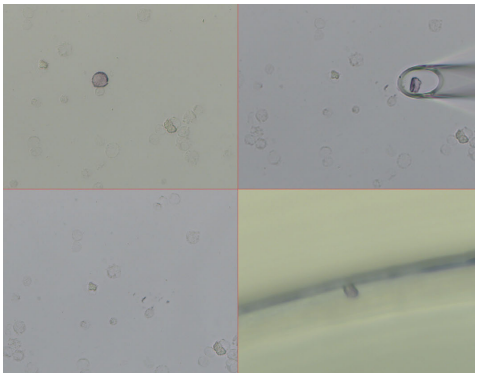
107C - uncertain



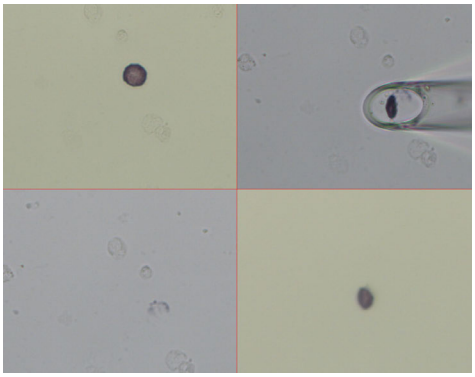
107D - TC



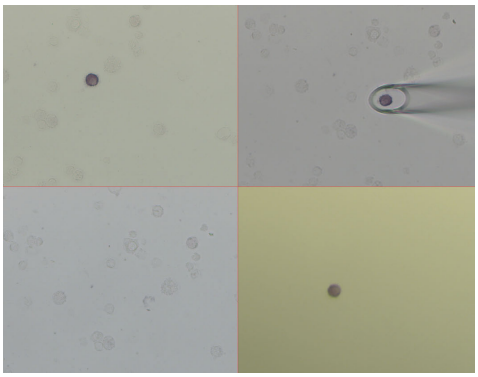
107E - TC



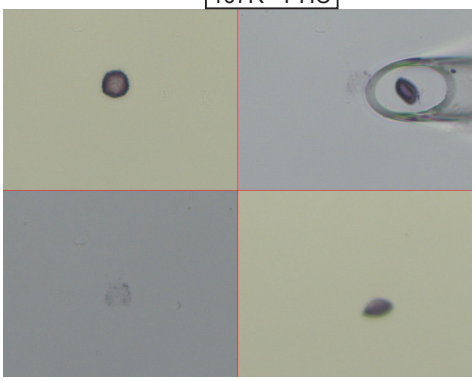
107F - PHC



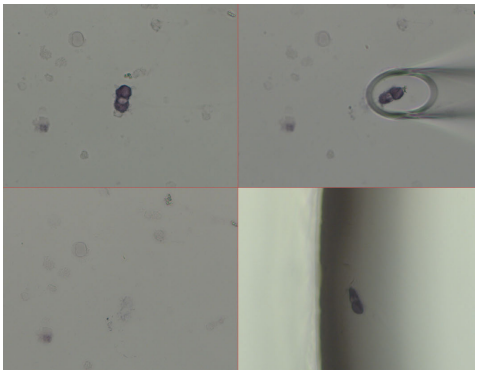
107G - PHC



107R - PHC

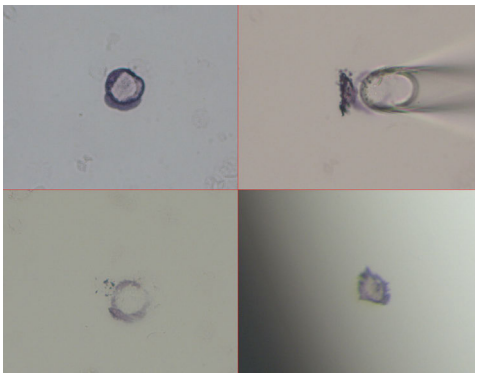


107S - uncertain

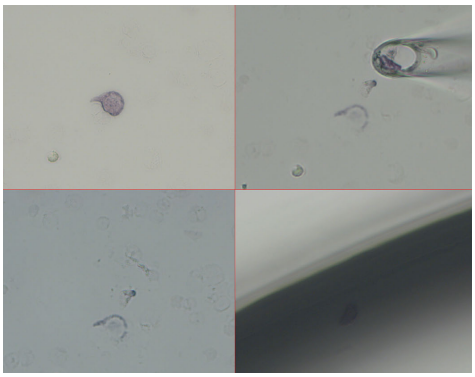


G

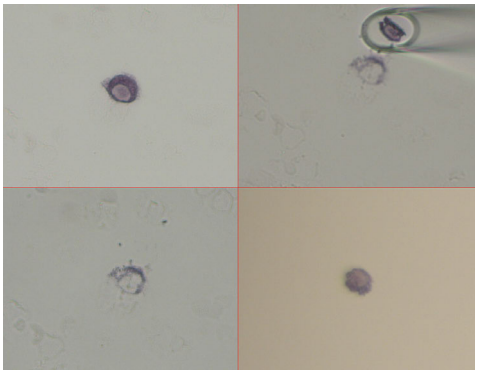
107H - TC



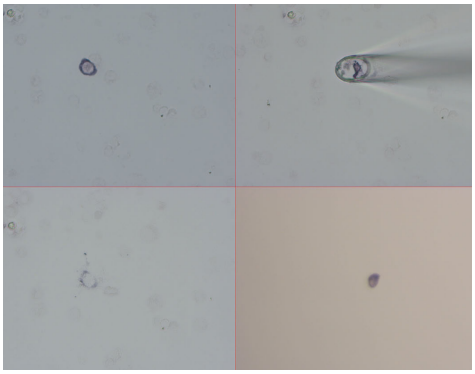
107I - TC



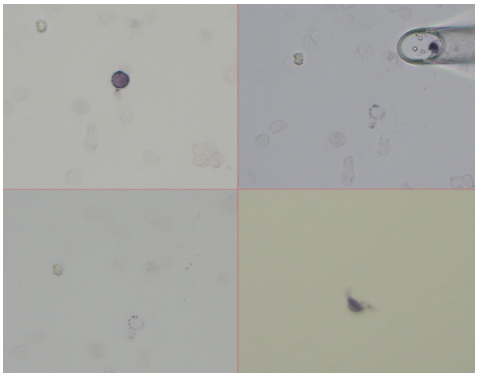
107J - HC



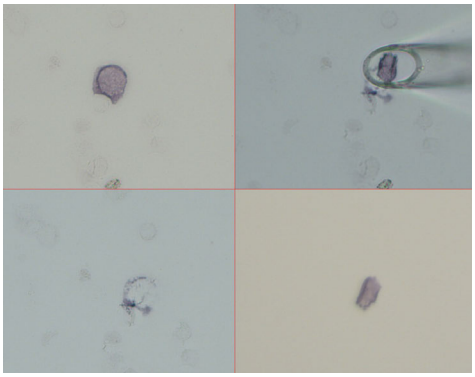
107K - TC



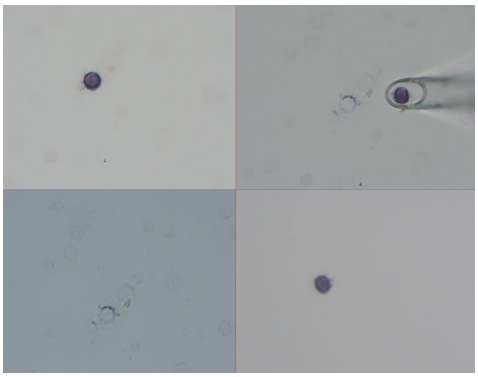
107L - TC



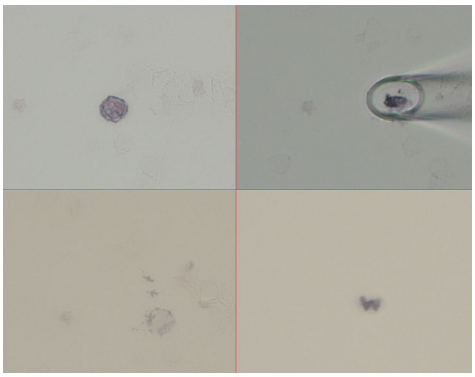
107M - TC



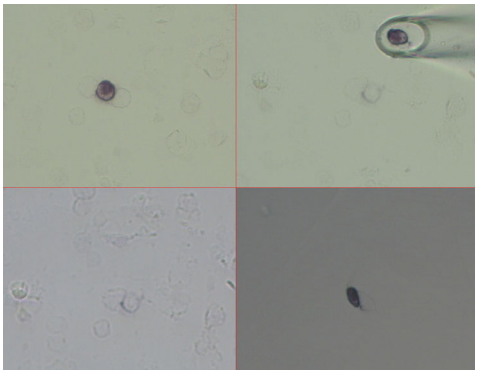
107N - TC



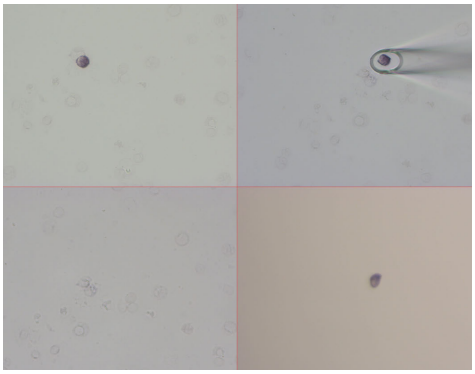
107O - TC



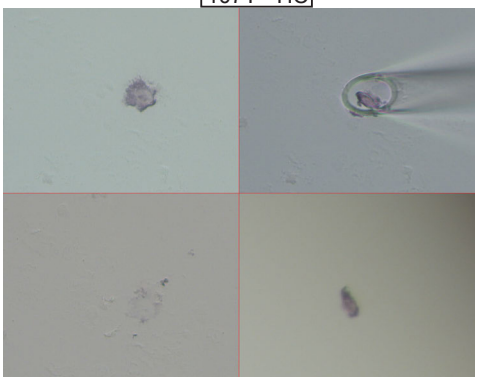
107P - TC



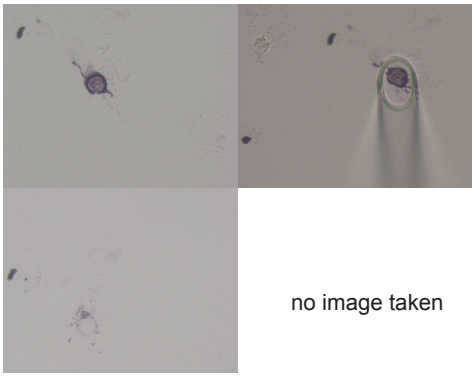
107Q - uncertain



107T - HC



107U - TC



no image taken

Figure S2: Assessment of noise in single-cell logR profiles. Median Absolute Pairwise Difference (MAPD) values (Materials and methods) embody the noise in logR between two consecutive genomic bins genome wide. Red cells failed this QC filter.

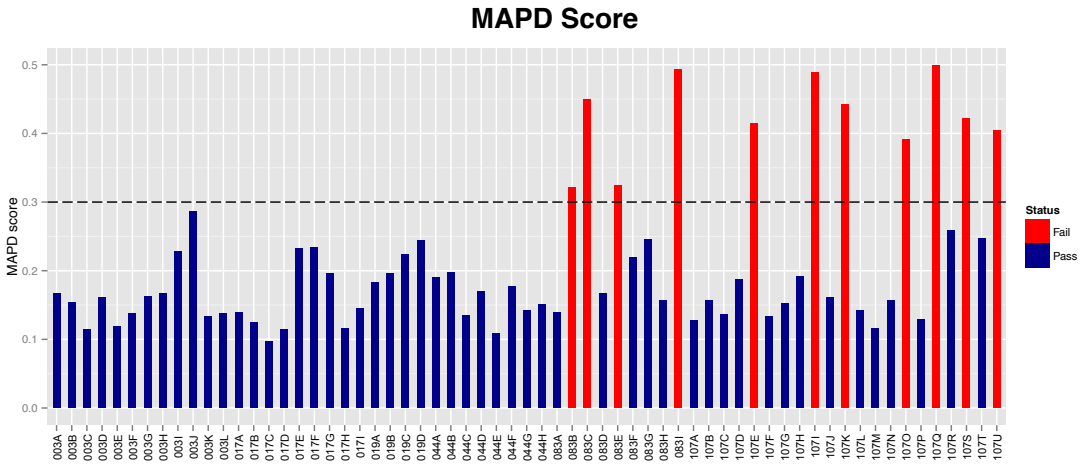


Figure S3: Focus on DNA copy number events overlapping in AUs and bulk tumor. (A-D) Per patient profiles are shown as concentric circles inside the circular human karyogram. Only those patients and regions that have overlapping CNAs between AUs and the tumor bulk are depicted. Total copy number is represented as a heat map from blue to red as indicated. Tumor samples and single cells are labeled on the corresponding circles and are color-coded: primary tumor bulk (PT) in cyan, lymph node bulk (LN) in purple, DTCs in orange, aberrant cells of unknown origin in dark green and Normal cells in green. Control cells are boxed. Panels are shown for patient MicMa017 (A), MicMa019 (B), MicMa044 (C) and MicMa107 at the time of diagnosis (D).

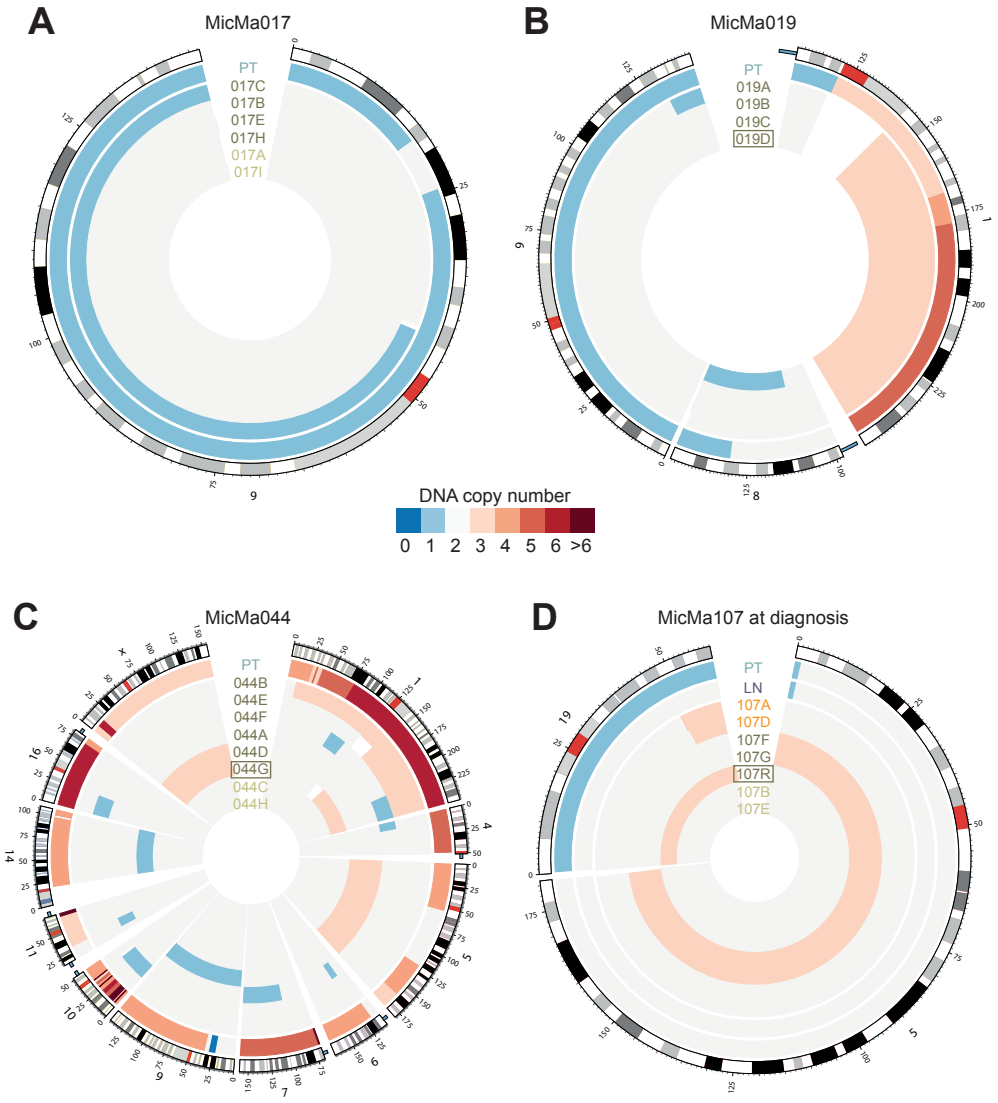


Figure S4: LogR profile of a 'Doublet' and two single cells. Genome-wide logR segments of 3 DTCs (003C, 003D, 003E) of patient MicMa003. Red and black depict logR segments obtained from single DTCs 003C and 003E, respectively, while blue indicates the logR segments of a doublet (003D).

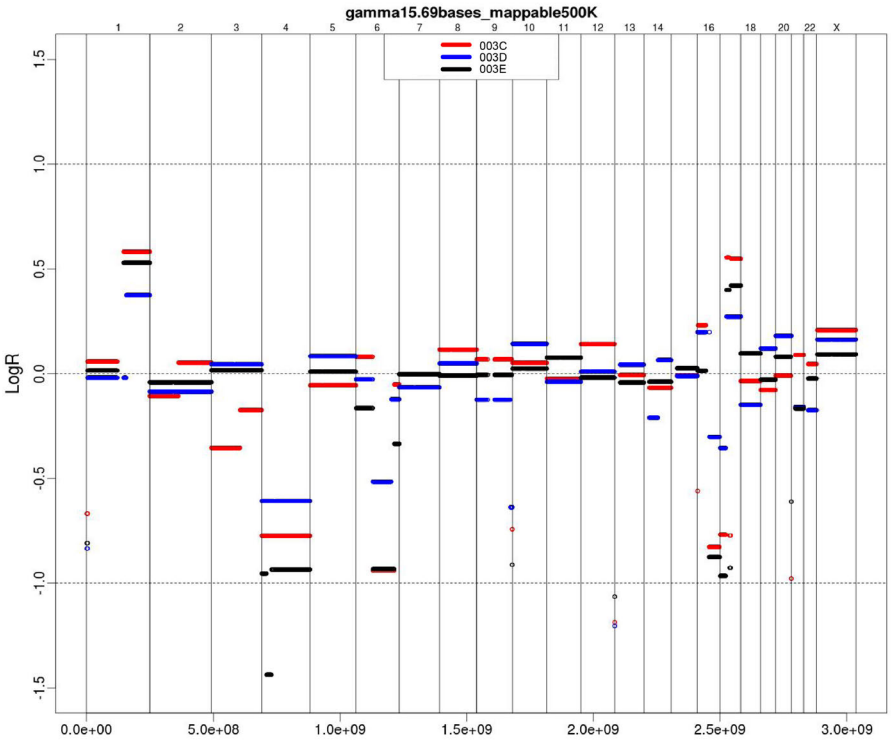


Figure S5: Retrospective power analysis. The cumulative number of unique CNAs is plotted as a function of the cumulative number of single cells for each sample. Mean and standard deviations of 100,000 randomized orders are shown. AD, at diagnosis; 3Y, 3 years after diagnosis.

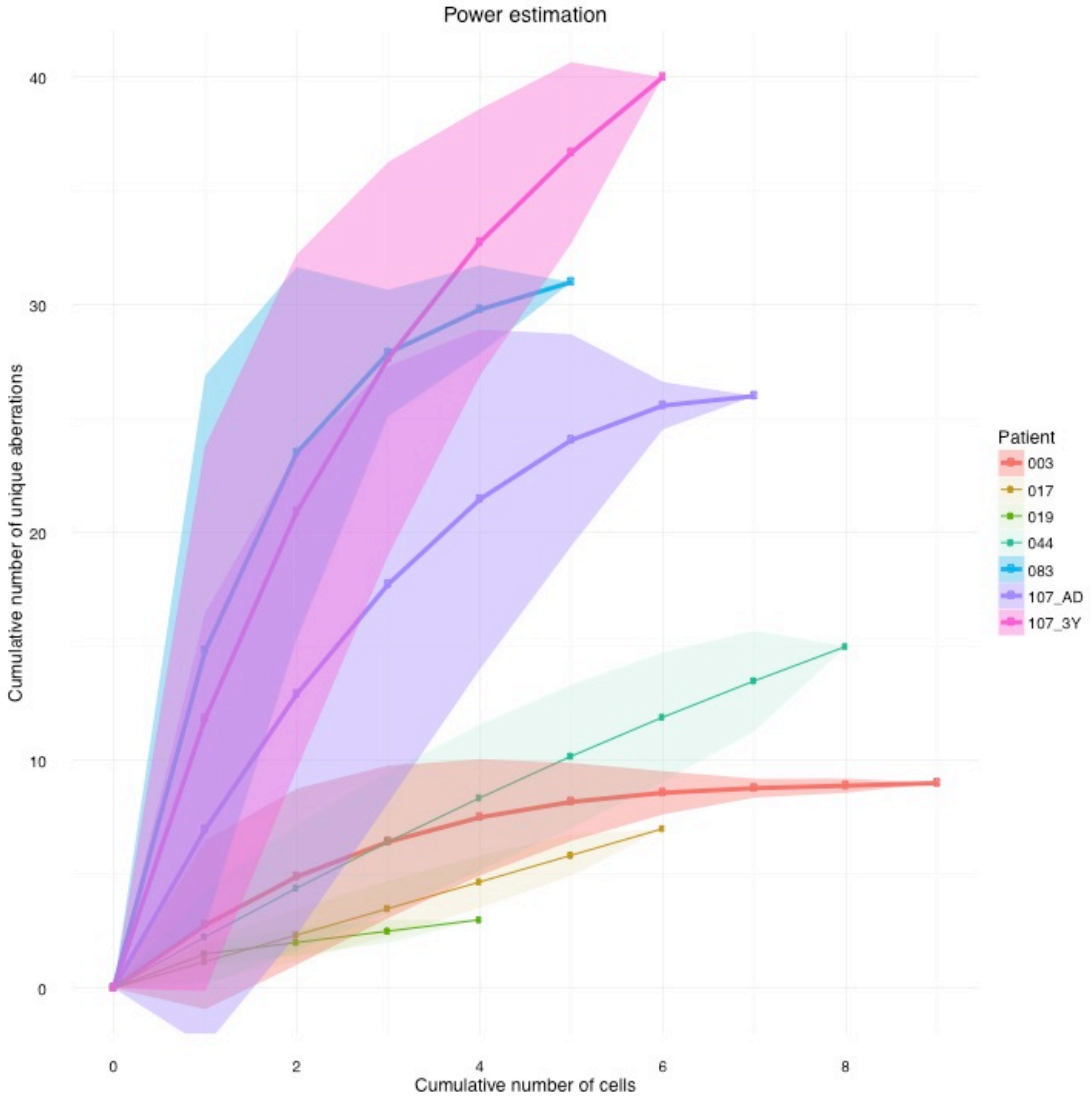


Figure S6: Coverage statistics of bulk exome sequences for all tumors and matched normal blood samples. The breadth of coverage across the exome (Y-axis) is depicted for different sequence depth cutoffs (X-axis). Primary tumor (PT), lymph node metastasis (LN) and matched blood (B).

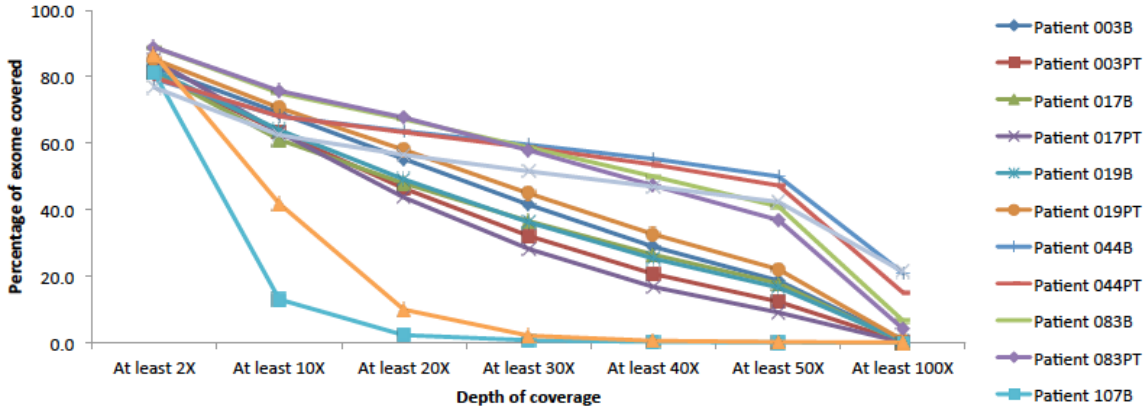


Figure S7: Genotyping of single nucleotide variants from bulk tumor exome sequences in the Doublet sequences. (A, B) Heat maps per tumor, where each row represents either a single somatic substitution called on the corresponding bulk exome and the matched blood (A), or a random heterozygous germline SNP (20 total, B), and columns represent the different Doublet or exome datasets obtained for that tumor. Tile colors reflect the presence of the mutant allele (orange), its absence (reference, blue), or whether there was no coverage at that position (white). (C) Modeled probability of observing an at least equally extreme pattern of somatic reference and variant alleles for that Doublet through false positives (none of the cells have any of the tumor's somatic mutations and hence derive from another lineage) or false negatives (at least one of the Doublet's cells derives from the tumor and hence contains these somatic mutations). Model results are encoded as heat maps of $-\log_{10}(p)$. For clarity, loci with zero coverage in all of the Doublets of that patient are omitted.

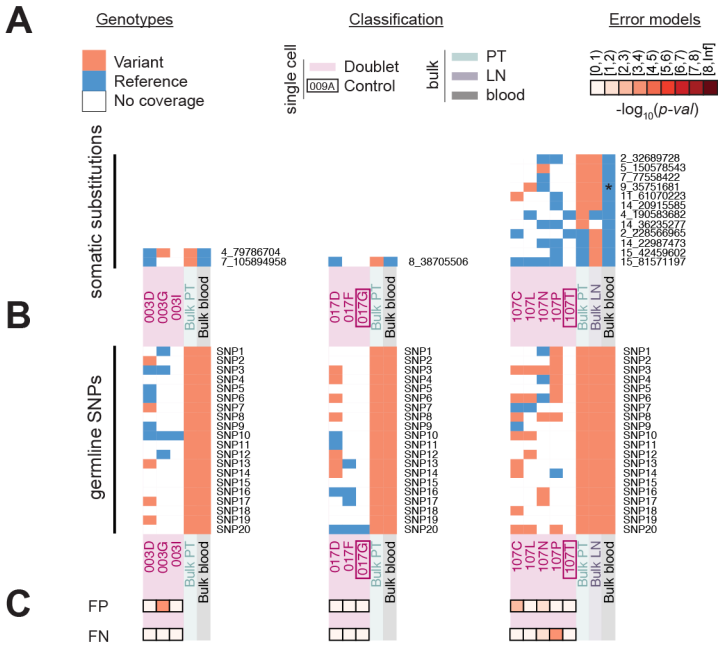
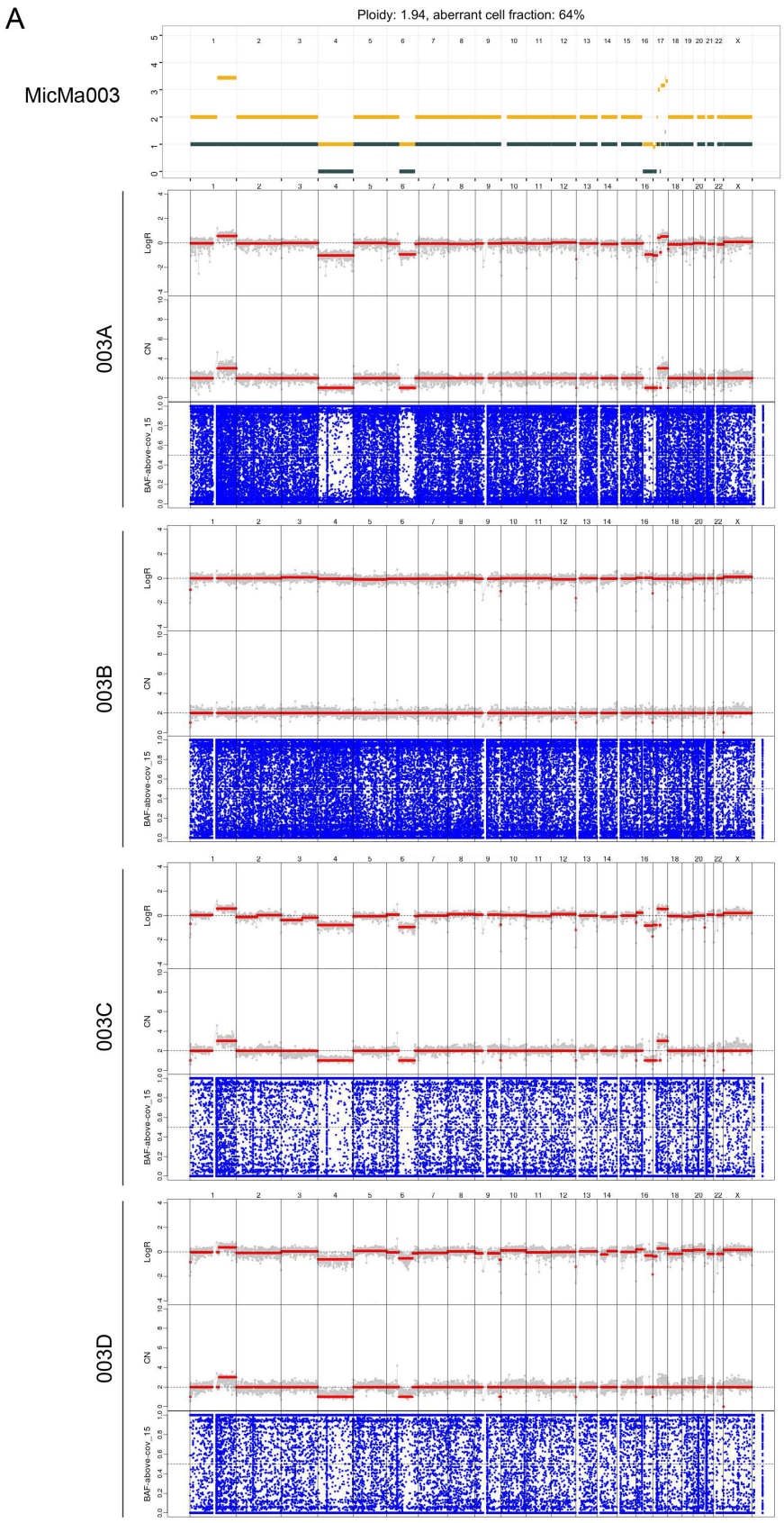
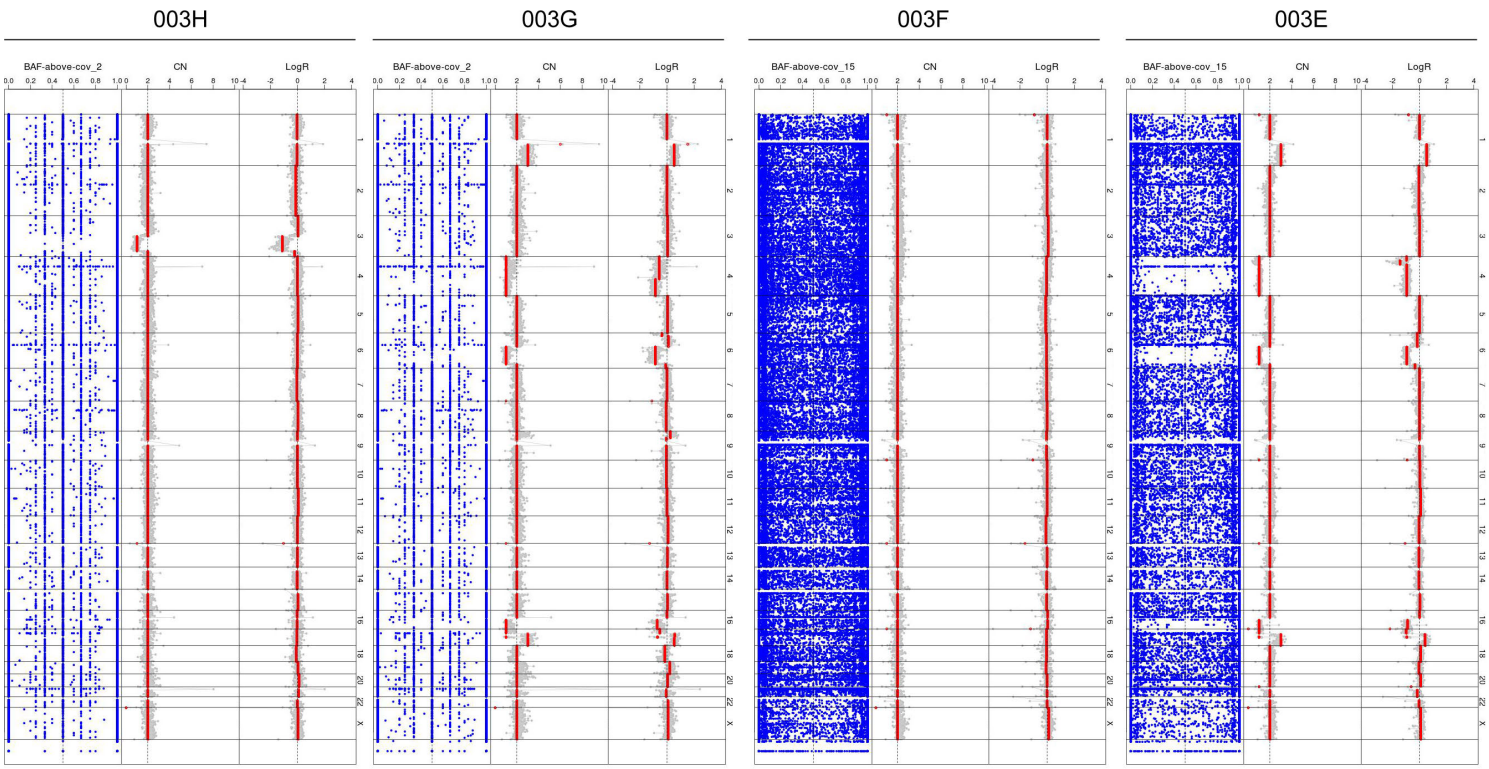
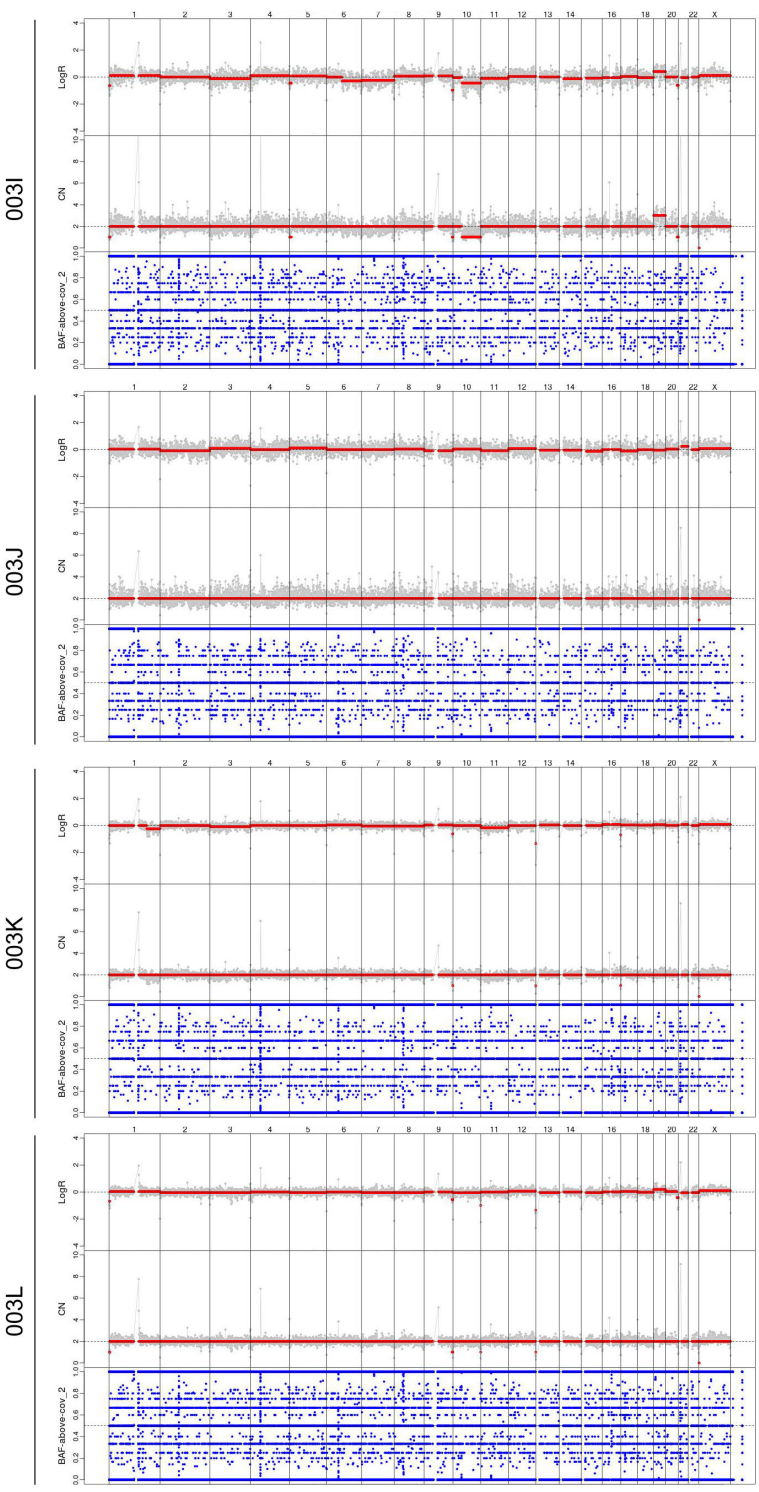
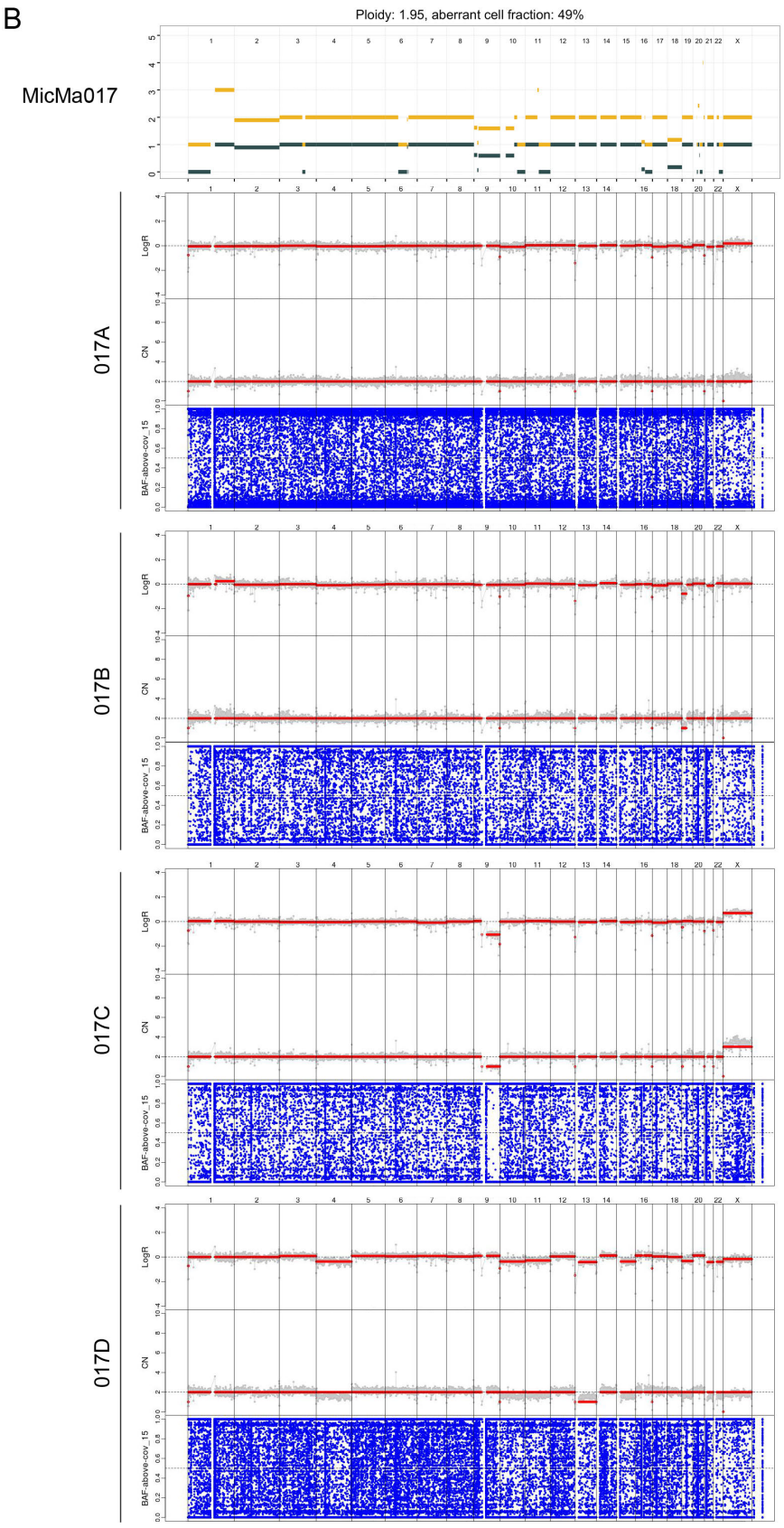


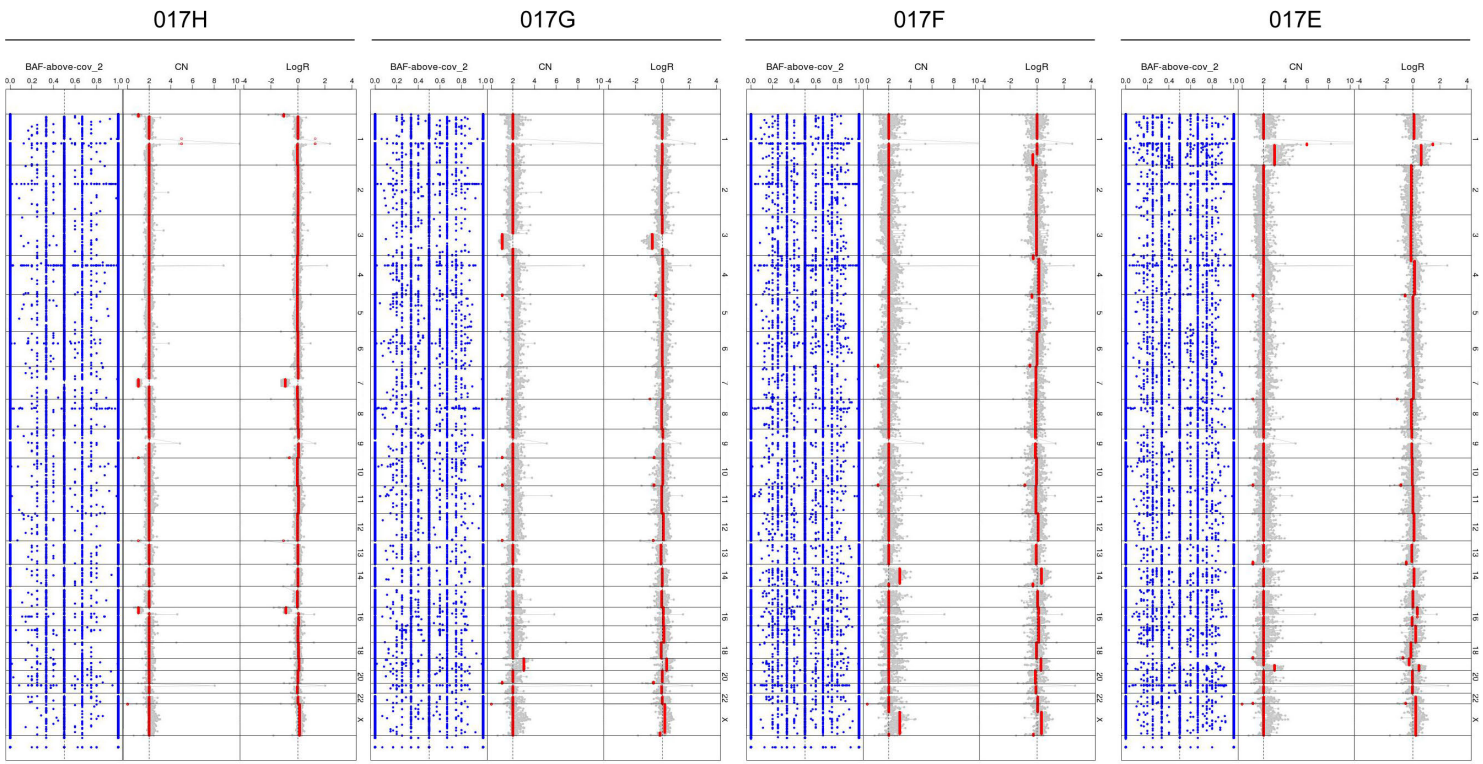
Figure S8: Tumor bulk copy number profiles and logR, copy number and BAF data of single cells from the corresponding patient. Each panel highlights the bulk copy number profile (on top) and single cell data (bottom) for a single patient/time point: patient MicMa003 (A), MicMa017 (B), MicMa019 (C), MicMa044 (D), MicMa083 (E), MicMa107 at diagnosis (F) and 3 years post-diagnosis (G). The copy number profile(s) are the output of the Battenberg algorithm based on the SNP-array data of bulk tumor DNA. Yellow indicates the total copy number, black the copy number of the minor allele. Regions with subclonal aberrations are evidenced by a non-integer copy number state. For each corresponding single cell, the logR, fitted copy number and BAF are plotted across the genome.

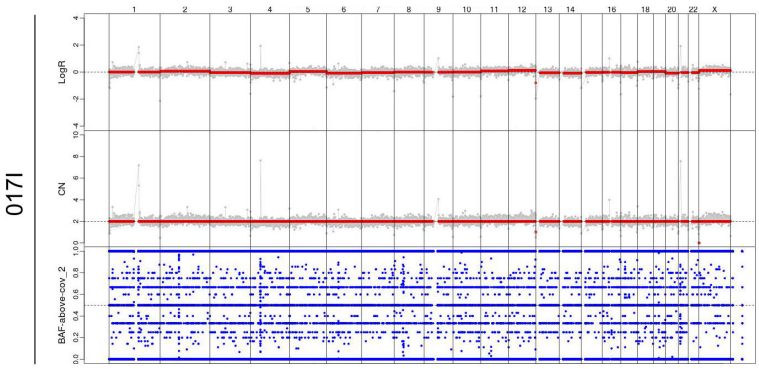

A
MicMa003
Ploidy: 1.94, aberrant cell fraction: 64%
003A
003B
003C
003D
LogR
CN
BAF-above-cov_15

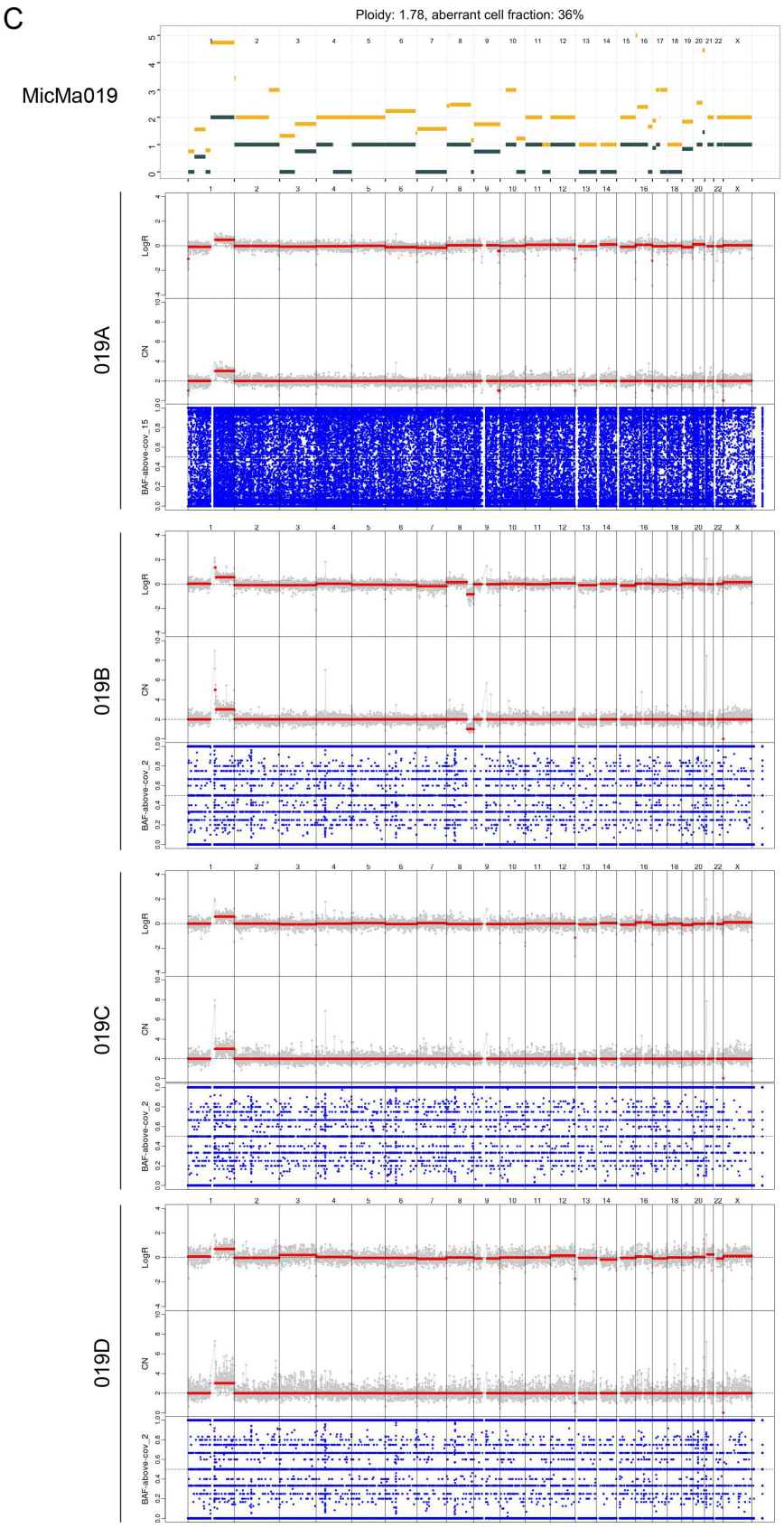

003H
003G
003F
003E
BAF-above-cov_2
BAF-above-cov_15
CN
LogR


003I
003J
003K
003L
LogR
CN
BAF-above-cov_2
1
2
3
4
5
6
7
8
9
10
11
12
13
14
16
18
20
22
X


B
MicMa017
Ploidy: 1.95, aberrant cell fraction: 49%
017A
017B
017C
017D
LogR
CN
BAF-above-cov_15

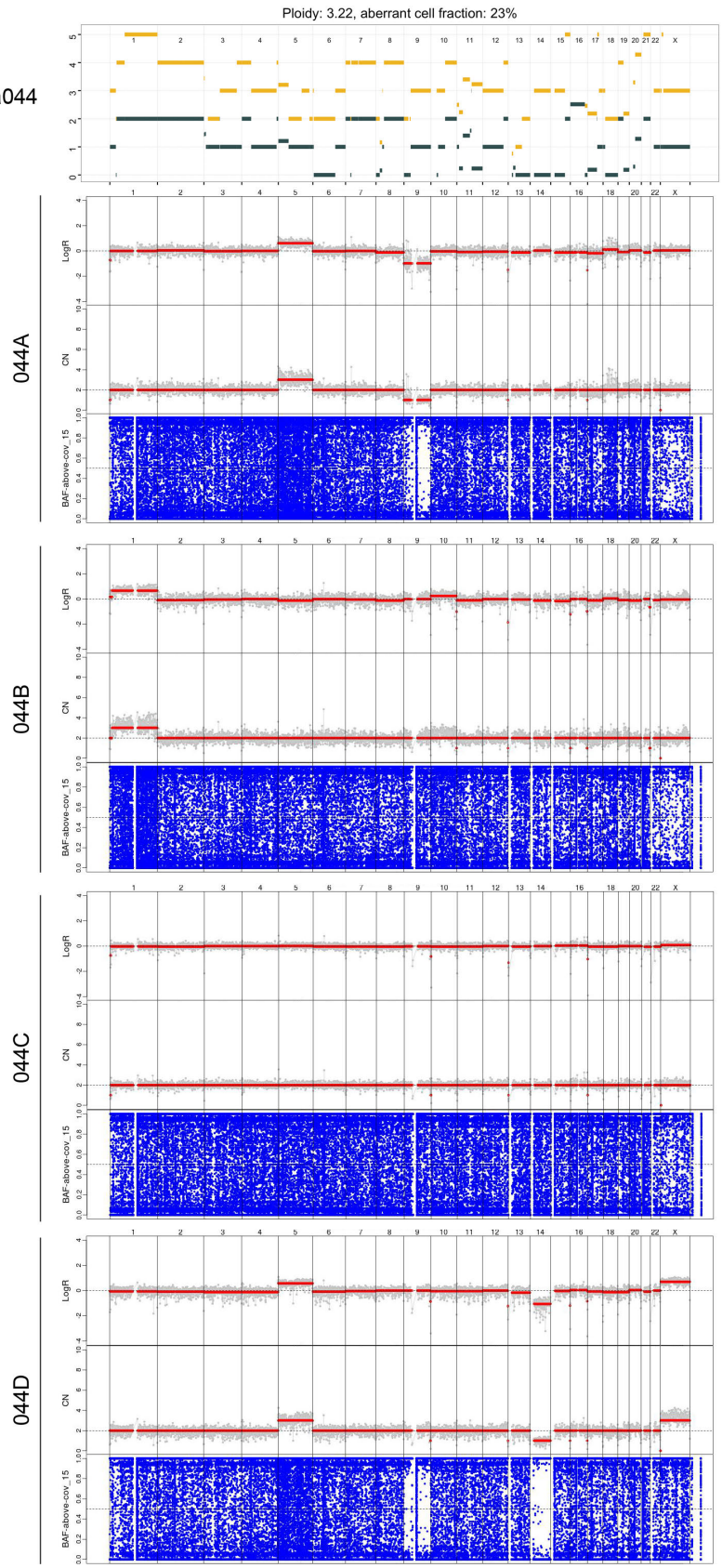

017H
017G
017F
017E
BAF-above-cov_2
CN
LogR

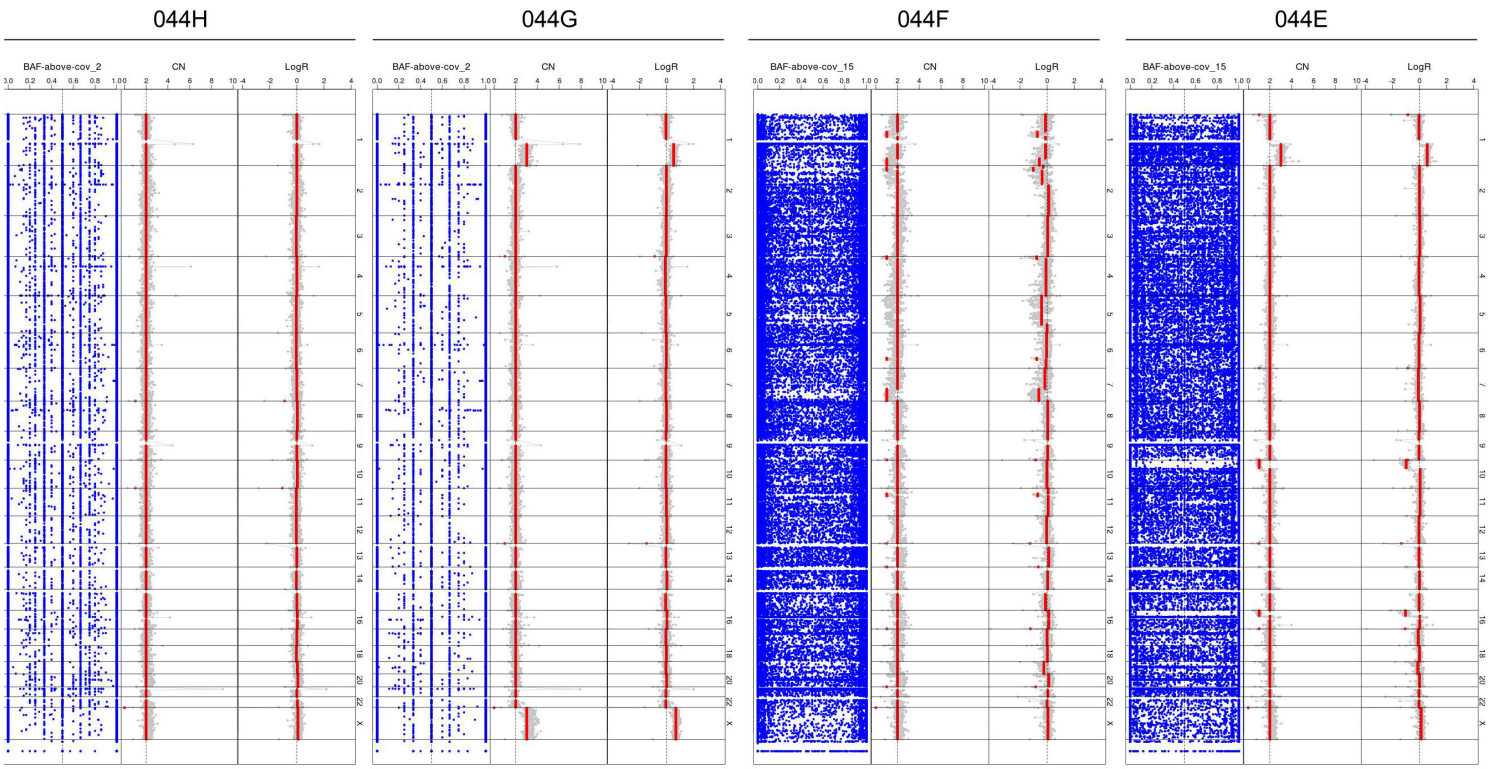

017I
1
2
3
4
5
6
7
8
9
10
11
12
13
14
16
18
20
22
X
LogR
CN
BAF-above-cov_2

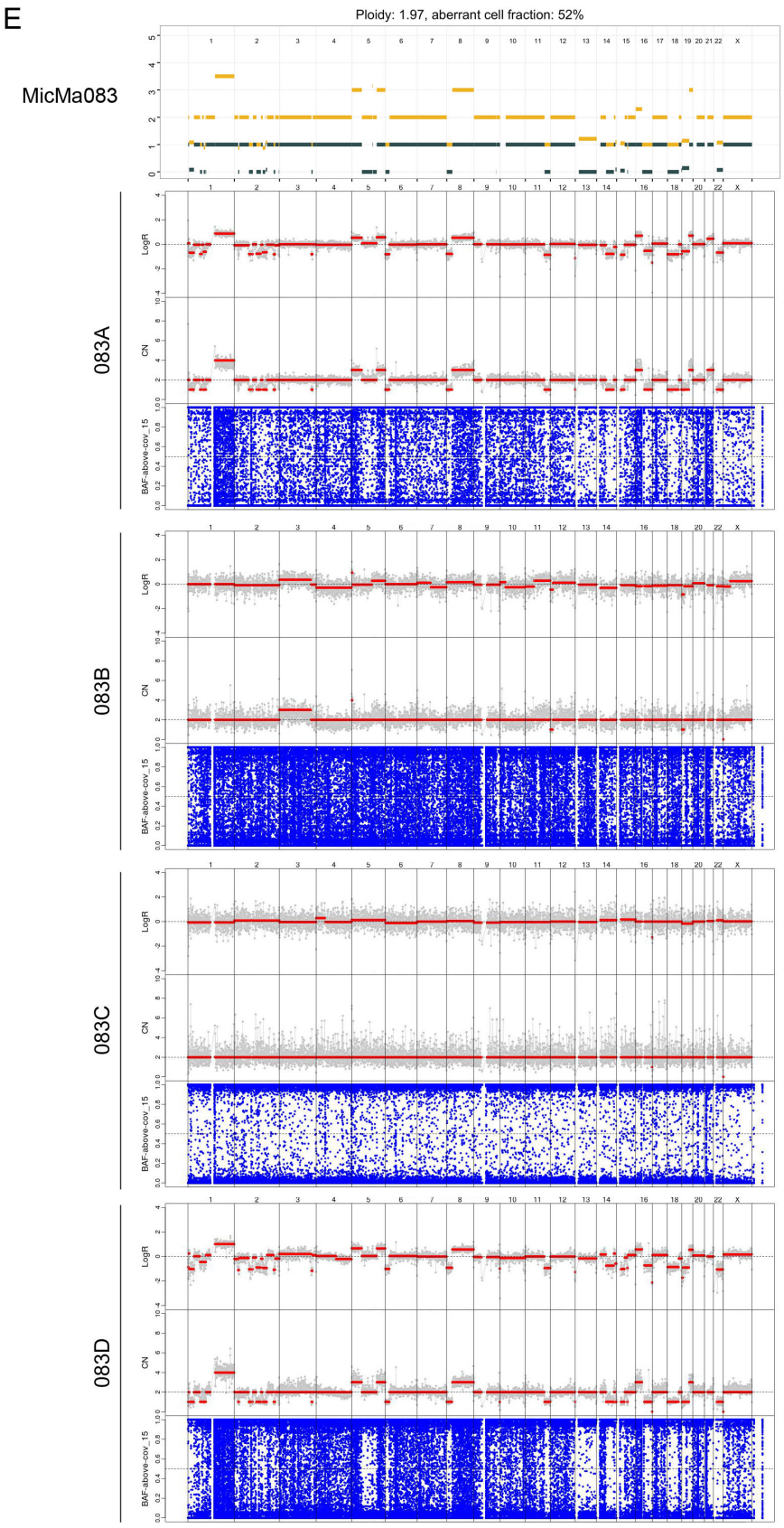

C
MicMa019
Ploidy: 1.78, aberrant cell fraction: 36%
019A
019B
019C
019D
LogR
CN
BAF-above-cov_15
BAF-above-cov_2

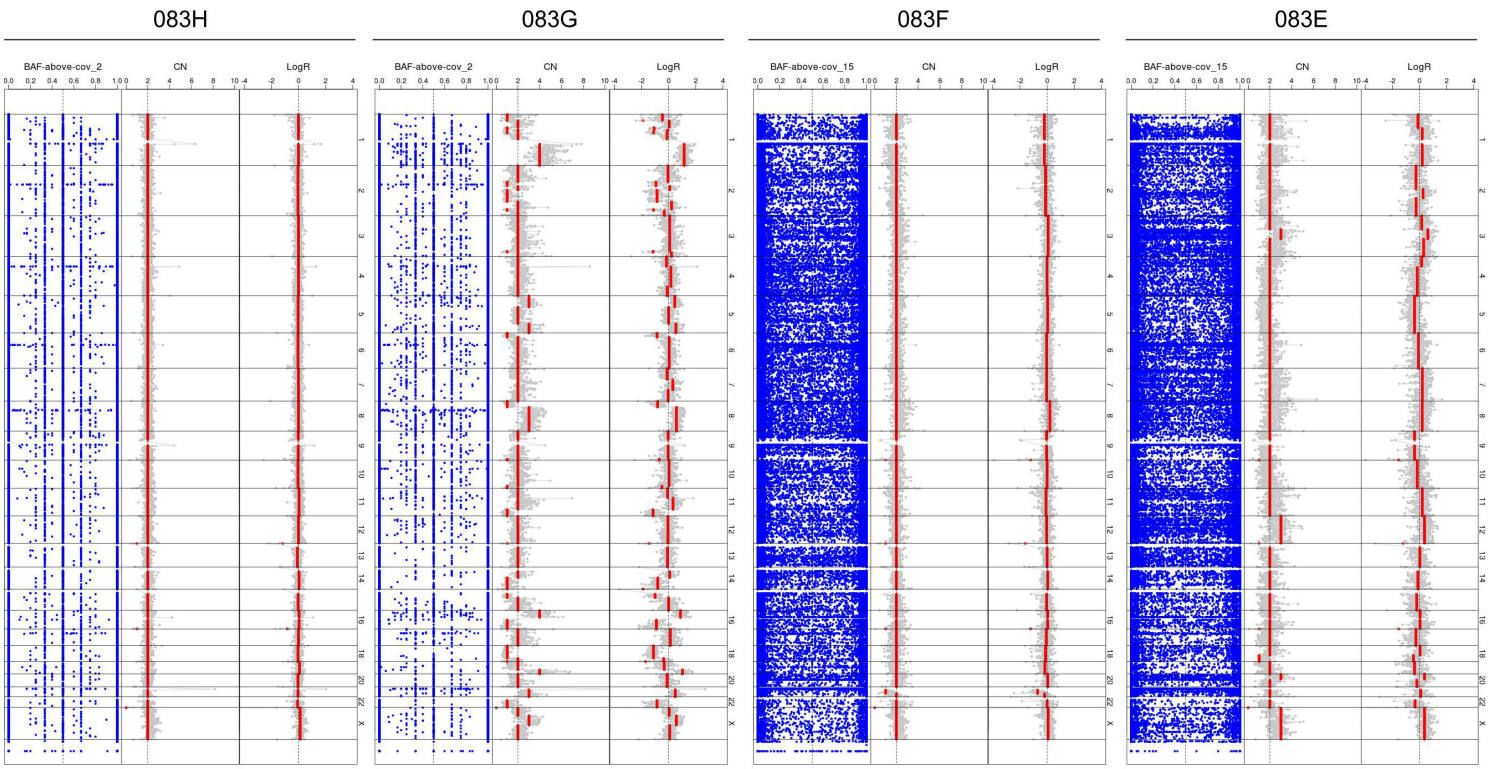
D

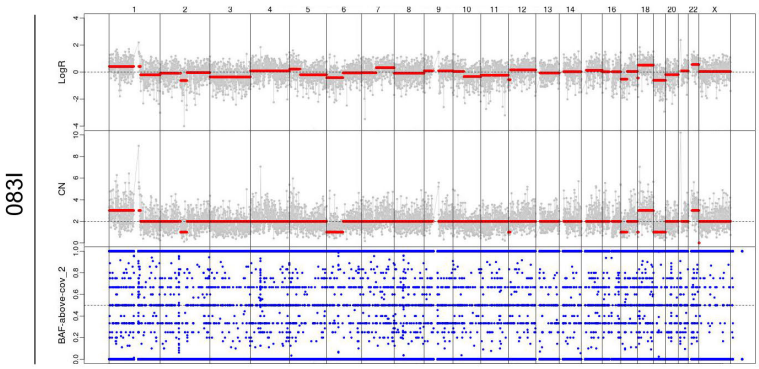
MicMa044


Ploidy: 3.22, aberrant cell fraction: 23%
044A
044B
044C
044D
LogR
CN
BAF-above-cov_15


044H
044G
044F
044E
BAF-above-cov_2
BAF-above-cov_15
CN
LogR


E
MicMa083
Ploidy: 1.97, aberrant cell fraction: 52%
083A
083B
083C
083D
LogR
CN
BAF-above-cov_15


083H
083G
083F
083E
BAF-above-cov_2
BAF-above-cov_15
CN
LogR


083I
1
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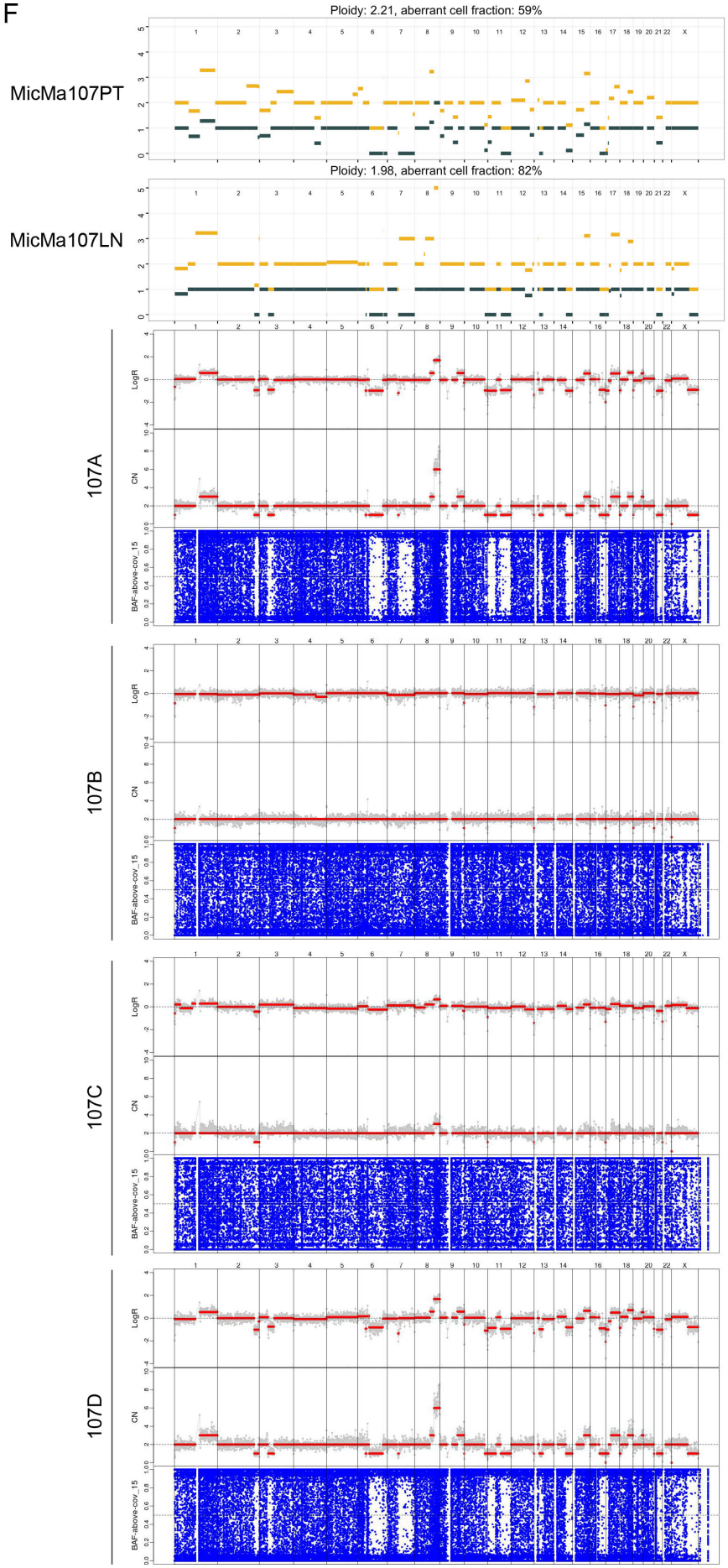
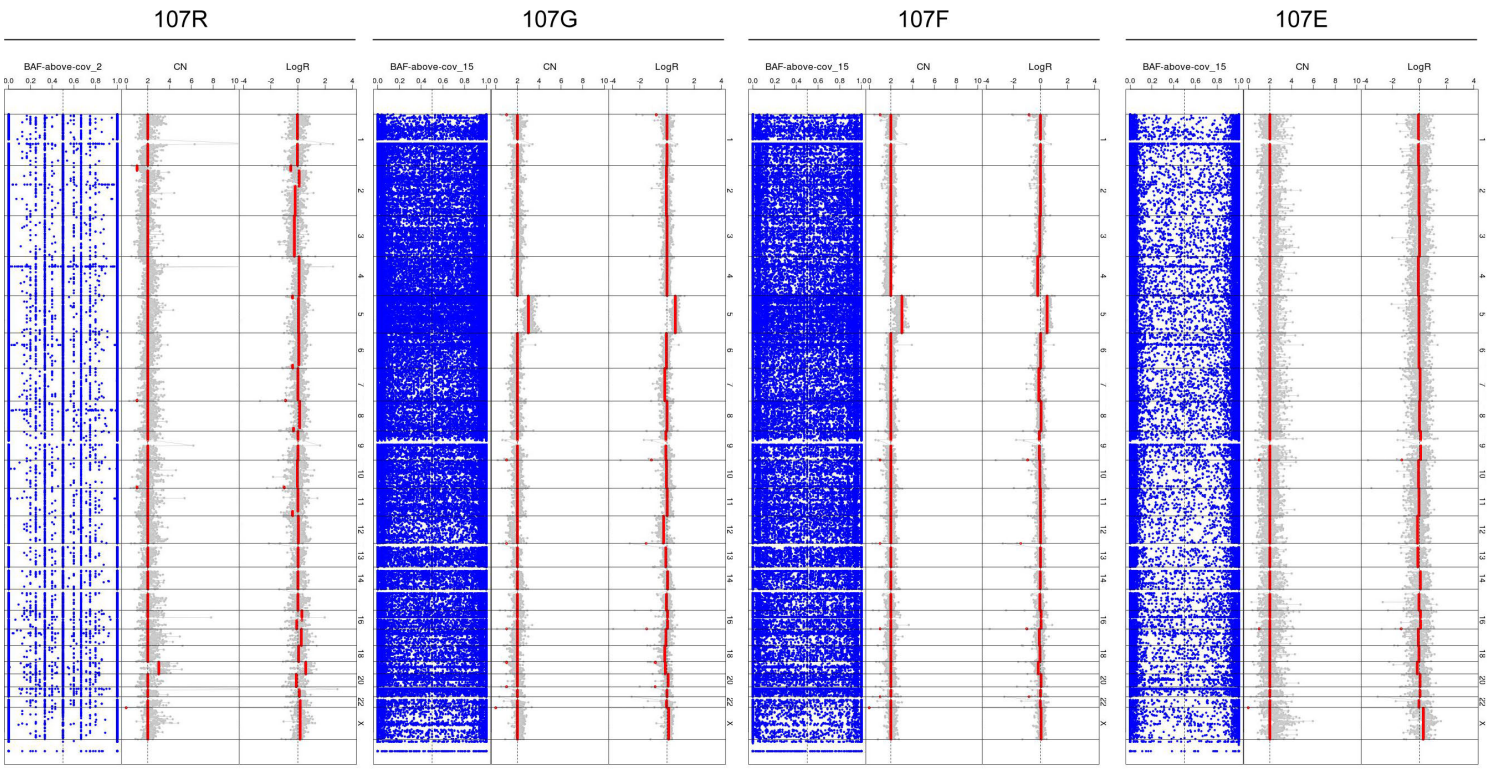
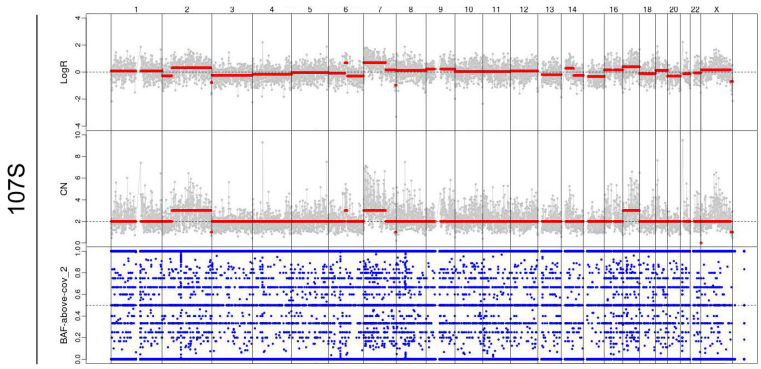
14
16
18
20
22
X
LogR
CN
BAF-above-cov_2

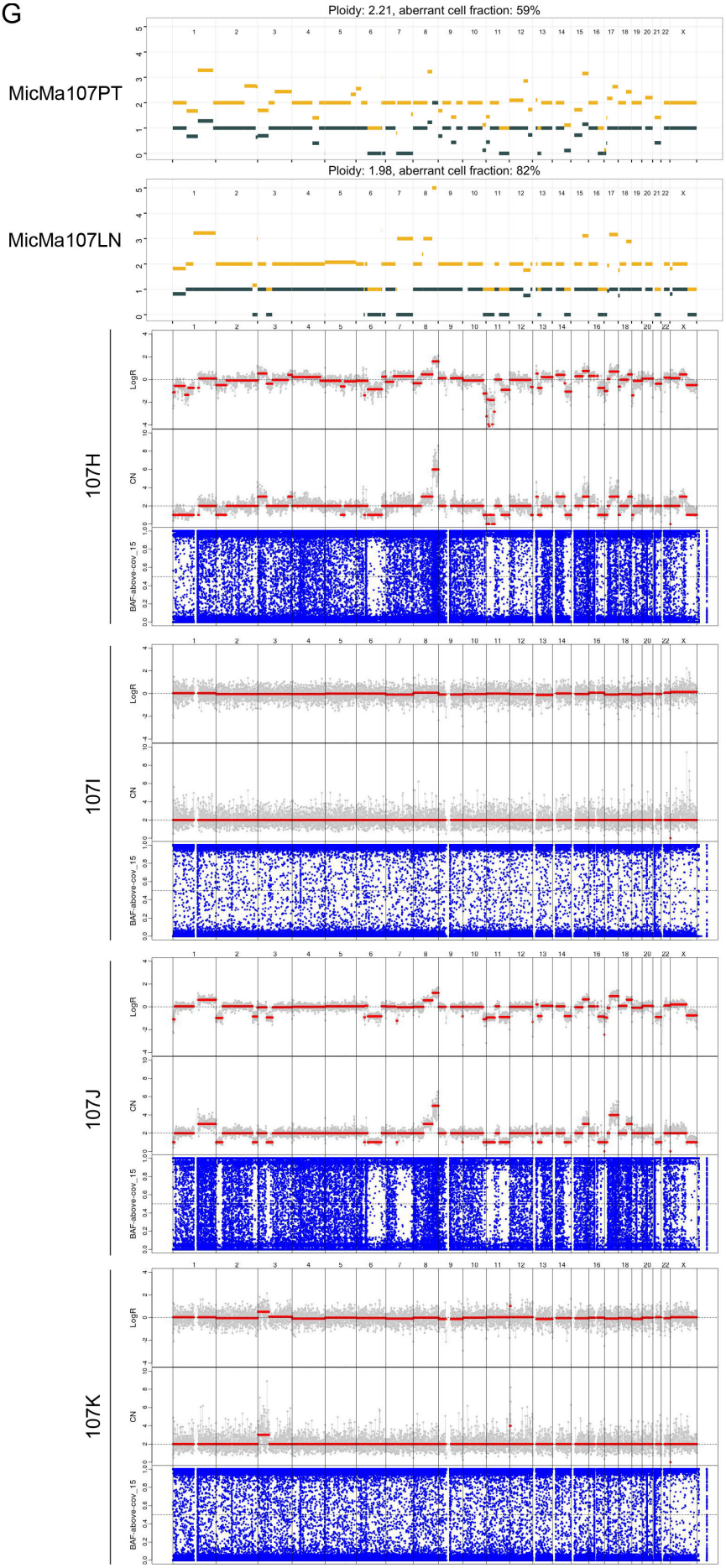
F

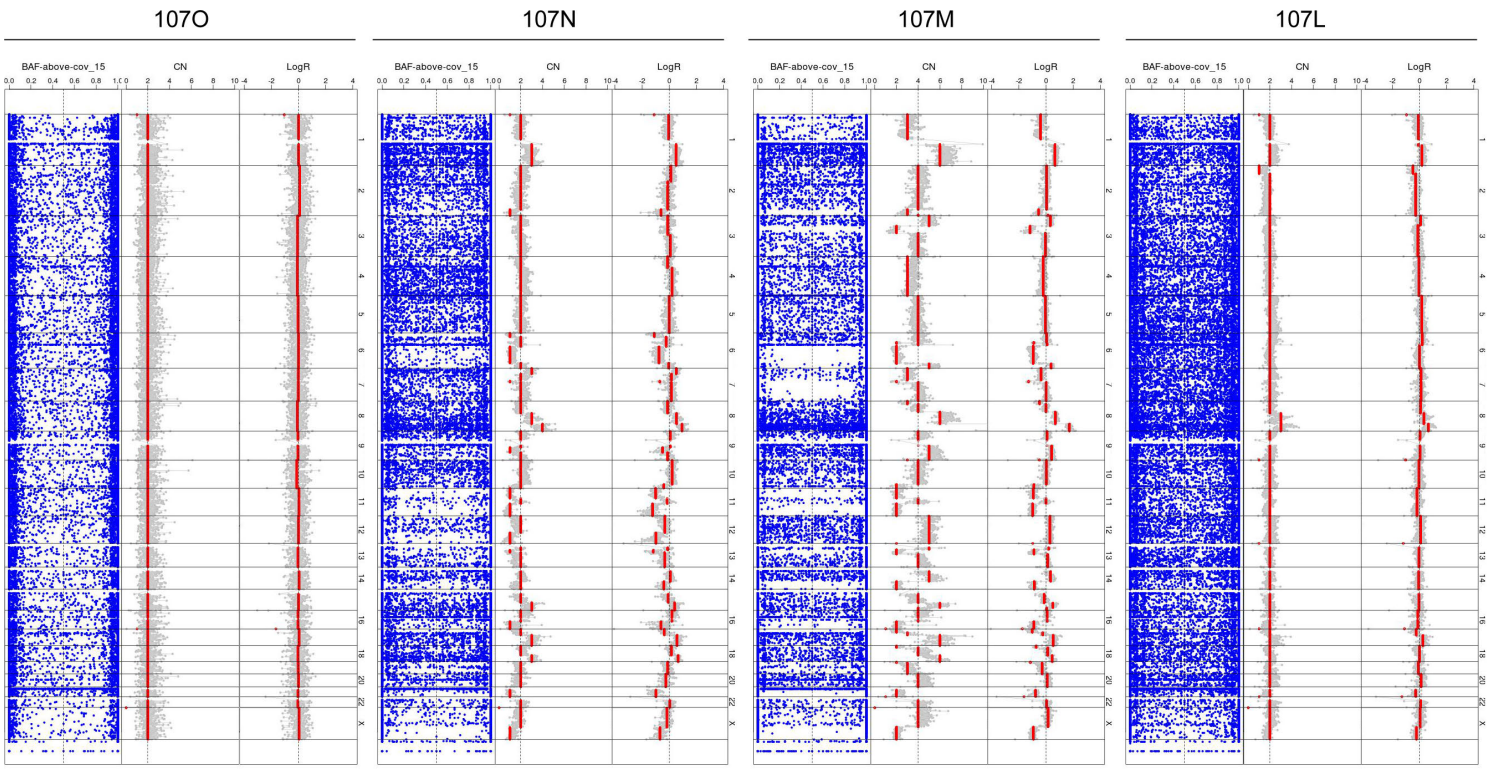

MicMa107PT
Ploidy: 2.21, aberrant cell fraction: 59%
MicMa107LN
Ploidy: 1.98, aberrant cell fraction: 82%
107A
107B
107C
107D
LogR
CN
BAF-above-cov_15


107R
107G
107F
107E
BAF-above-cov_2
BAF-above-cov_15
CN
LogR


107S
1
2
3
4
5
6
7
8
9
10
11
12
13
14
16
18
20
22
X
LogR
CN
BAF-above-cov_2

G


MicMa107PT
Ploidy: 2.21, aberrant cell fraction: 59%
MicMa107LN
Ploidy: 1.98, aberrant cell fraction: 82%
107H
107I
107J
107K
LogR
CN
BAF-above-cov_15


107O
107N
107M
107L
BAF-above-cov_15
CN
LogR

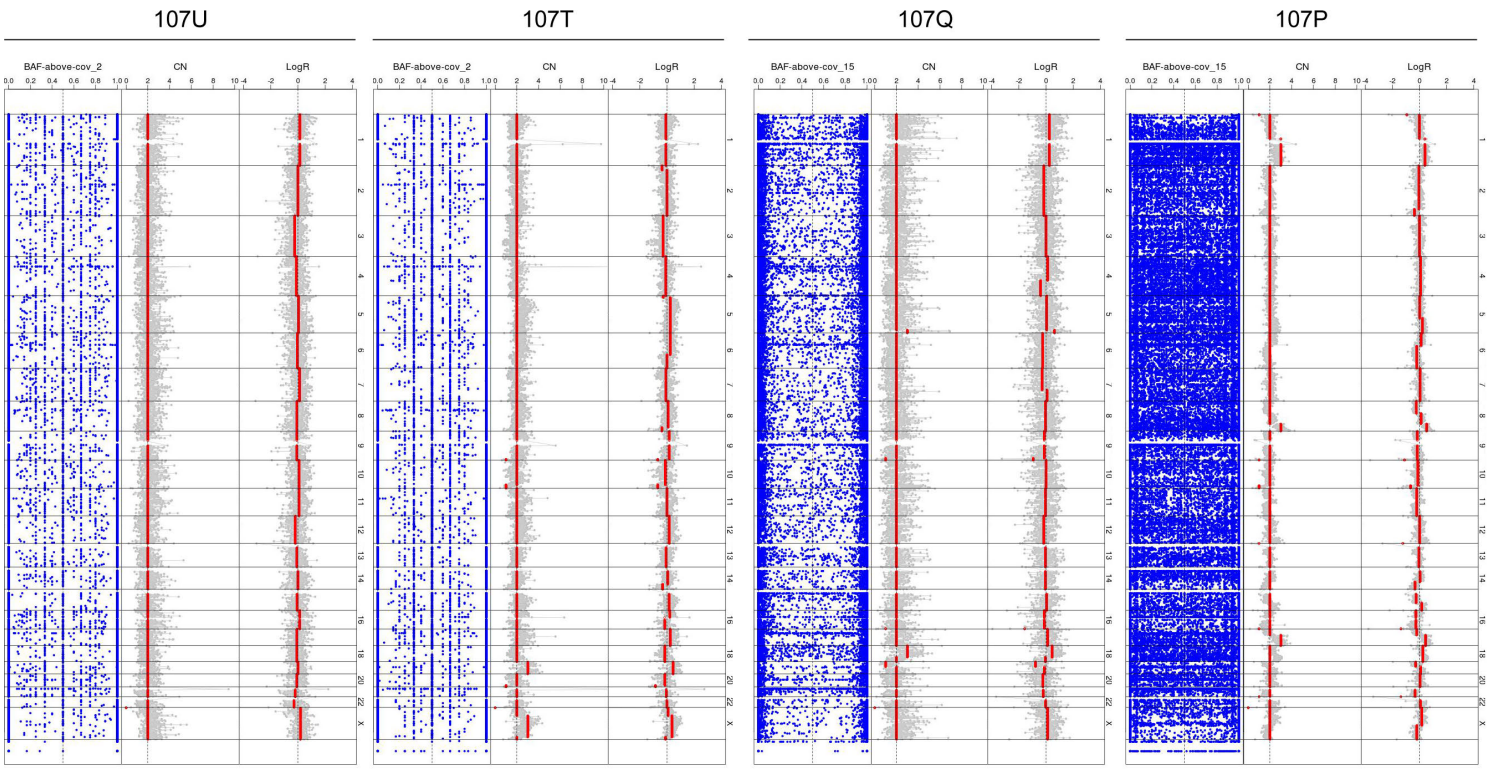
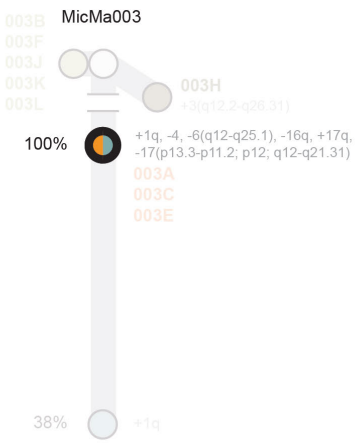
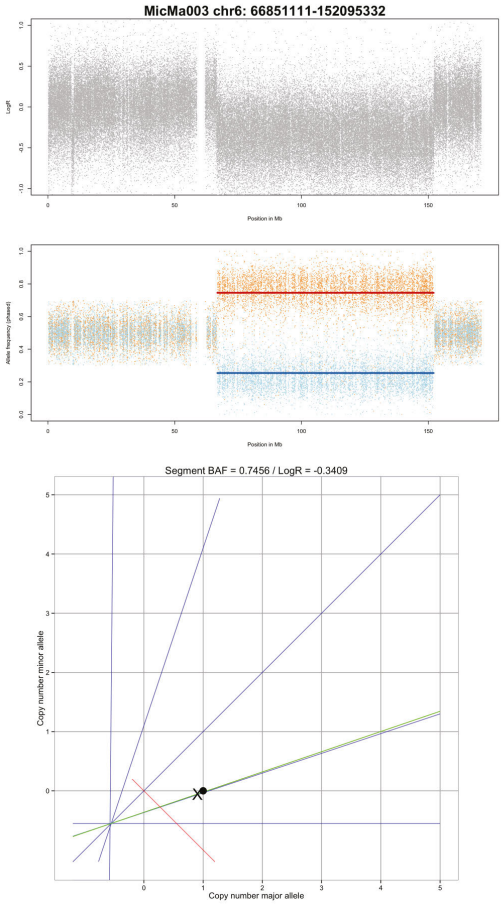
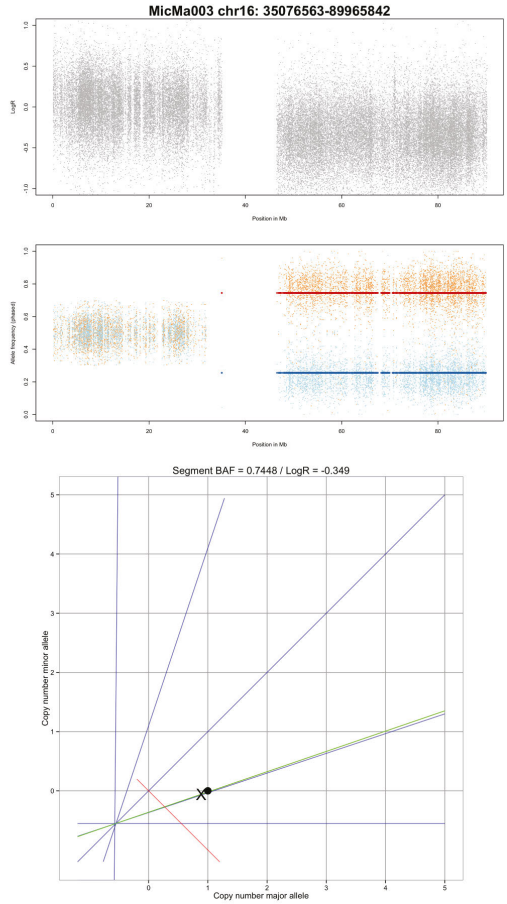

107U
107T
107Q
107P
BAF-above-cov_2
BAF-above-cov_15
CN
LogR

Figure S9: Battenberg bulk tumor results for phylogenetically informative segments. Each panel highlights a single node in the phylogenetic tree for the indicated patient (MicMa003, 083 or 107, top) and one or two evidencing segments as derived by Battenberg from the SNP6-array data from the primary tumor or lymph node metastasis (bottom). Battenberg plots represent the logR (top) and fitted segmented allele frequency for the relevant chromosome (middle), and the inferred (sub)clonal copy number state (bottom). The latter plot shows a grid of copy number states for the major (n_{Maj}) and minor (n_{Min}) alleles in the tumor. Blue lines are lines of equal BAF (0, 0.25, 0.5, 0.75 and 1) and red lines of equal logR in the copy number space. Using the estimated tumor purity (ρ) and ploidy (ψ_t) according to $n_{Maj} = \frac{\rho - 1 + 2^{\frac{r}{\gamma}} b(2(1-\rho)+\rho\psi_t)}{\rho}$ and $n_{Min} = \frac{\rho - 1 + 2^{\frac{r}{\gamma}} (1-b)(2(1-\rho)+\rho\psi_t)}{\rho}$, the measured logR ($r$) and B-allele frequency (b) correspond to a single point (plotted as 'X') in this copy number space ([38], Van Loo et al, *Proc Natl Acad Sci U S A*, 2011). The distance from this point to a clonal solution (i.e. the closest grid point) is checked via a standard t-test (black dot if clonal). If $p < 0.05$, a subclonal solution (the two red points) is proposed along one side of the copy number square containing the 'X' ([3], Nik-Zainal et al, *Cell*, 2012). The iso-BAF line corresponding to the segment's BAF (green) crosses two edges of the square, one of which is chosen based on whether the segment's logR is smaller or larger than the square's diagonal of constant logR. The cancer cell fractions are determined by the point of intersection between this edge and the line of equal BAF and are reflected by the size of the red points. Panels detail evidence for the MRCA (A) or the 38% subclone (B) in MicMa003; for the MRCA (C), the 50% (D), the 30% (E) or the 21% (F) subclone in MicMa083; for the MRCA (G), the 88% (H) or other subclones (I) in the primary of MicMa107; and for the MRCA (J), the 89% (K), the 39% (L), the 25% (M), the 16% (N) or other subclones (O) in the lymph node metastasis of MicMa107.

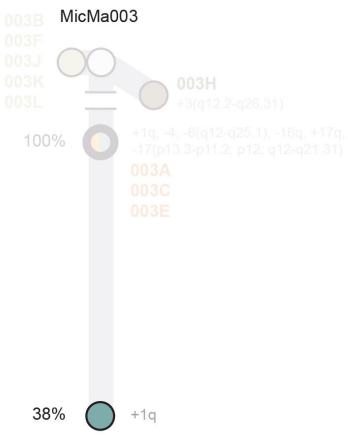
A

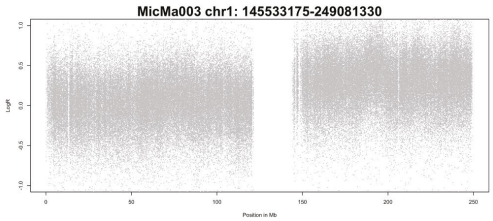

MicMa003
003B
003F
003J
003K
003L
003H
+3(q12.2-q26.31)
100%
+1q, -4, -6(q12-q25.1), -16q, +17q,
-17(p13.3-p11.2; p12; q12-q21.31)
003A
003C
003E
38%
+1q

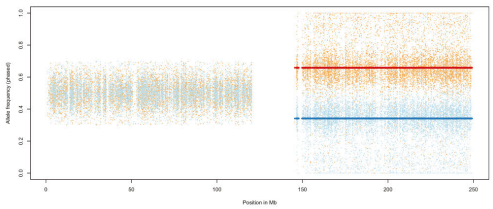

MicMa003 chr6: 66851111-152095332
LogR
Position in Mb
Allele frequency (Altered)
Segment BAF = 0.7456 / LogR = -0.3409
Copy number minor allele
Copy number major allele

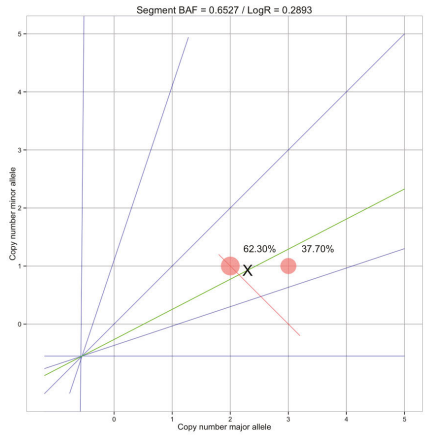

MicMa003 chr16: 35076563-89965842
LogR
Position in Mb
Allele frequency (Altered)
Segment BAF = 0.7448 / LogR = -0.349
Copy number minor allele
Copy number major allele

B

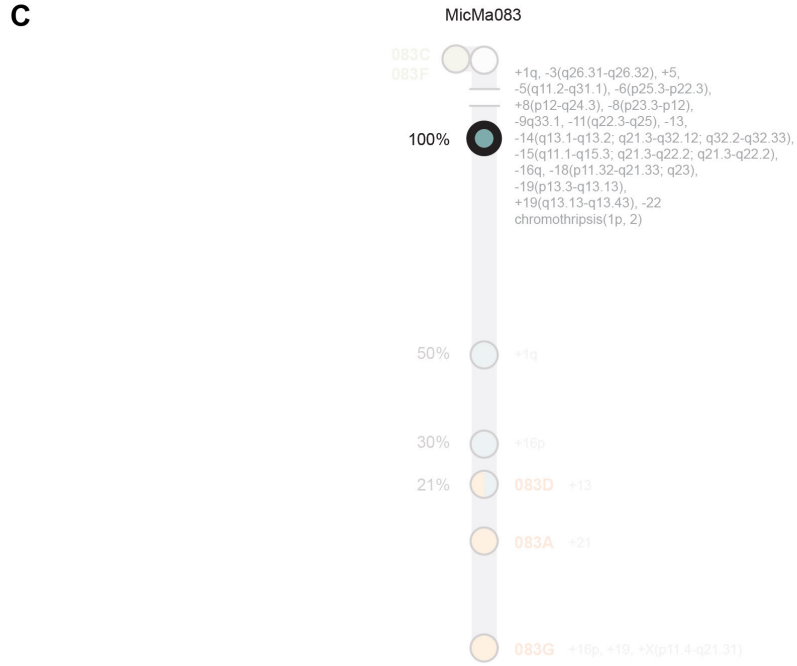

MicMa003
003B
003F
003J
003K
003L
003H
+3(q12.2-q28.31)
100%
+1q, -4, -6(q12-q25.1), -16q, +17q, -17(p13.3-p11.2; p12; q12-q21.31)
003A
003C
003E
38%
+1q

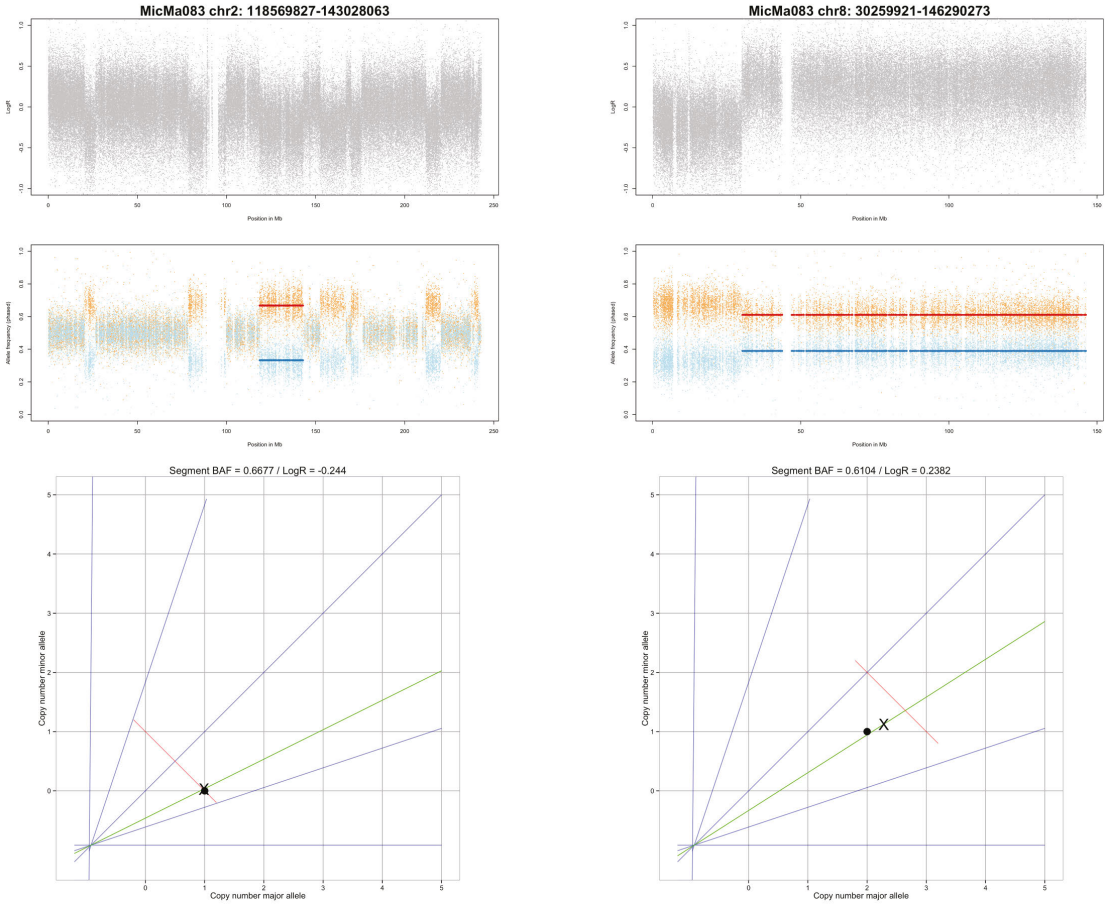

MicMa003 chr1: 145533175-249081330
LogR
Position in Mb


Allele frequency (phased)
Position in Mb

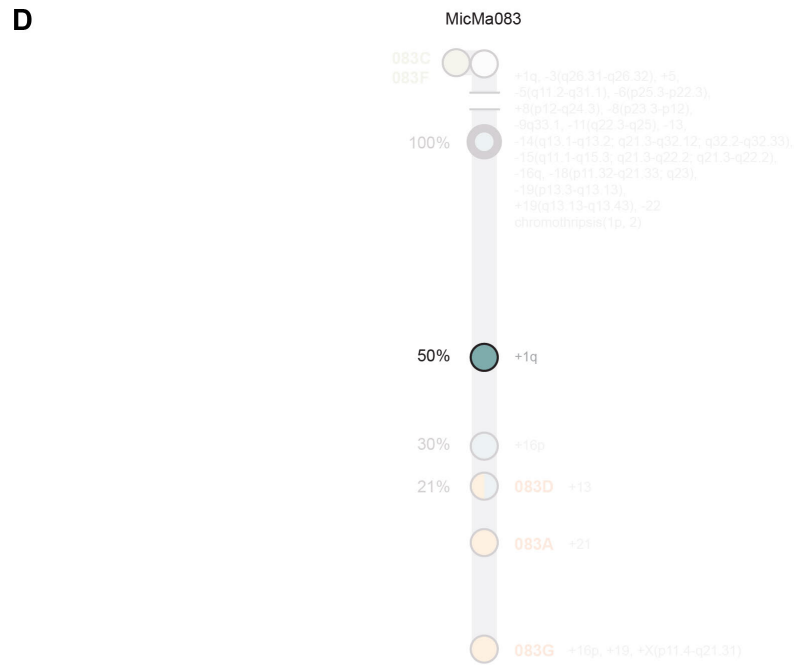

Segment BAF = 0.6527 / LogR = 0.2893
62.30%
37.70%
Copy number minor allele
Copy number major allele

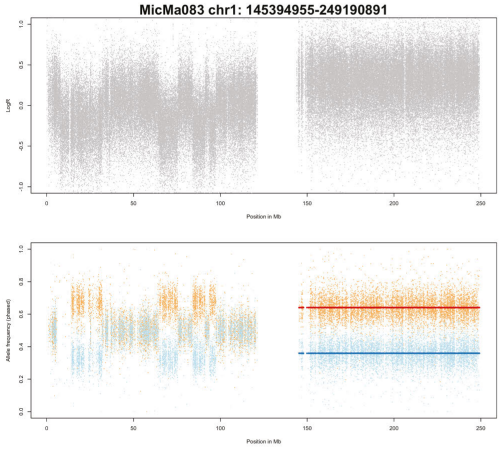
C

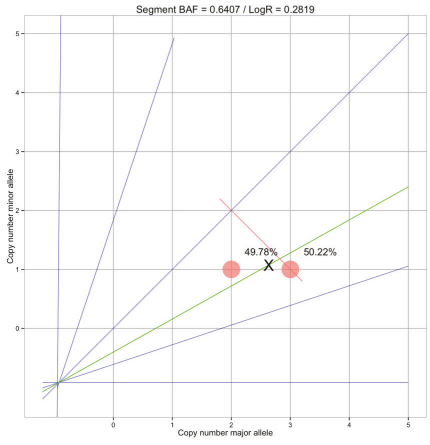

MicMa083
083C
083F
+1q, -3(q26.31-q26.32), +5,
-5(q11.2-q31.1), -6(p25.3-p22.3),
+8(p12-q24.3), -8(p23.3-p12),
-9q33.1, -11(q22.3-q25), -13,
-14(q13.1-q13.2; q21.3-q32.12; q32.2-q32.33),
-15(q11.1-q15.3; q21.3-q22.2; q21.3-q22.2),
-16q, -18(p11.32-q21.33; q23),
-19(p13.3-q13.13),
+19(q13.13-q13.43), -22
chromothripsis(1p, 2)
100%
50%
+1q
30%
+16p
21%
083D
+13
083A
+21
083G
+16p, +19, +X(p11.4-q21.31)


MicMa083 chr2: 118569827-143028063
MicMa083 chr8: 30259921-146290273
LogR
Position in Mb
Allele frequency (chasers)
Segment BAF = 0.6677 / LogR = -0.244
Segment BAF = 0.6104 / LogR = 0.2382
Copy number minor allele
Copy number major allele
X

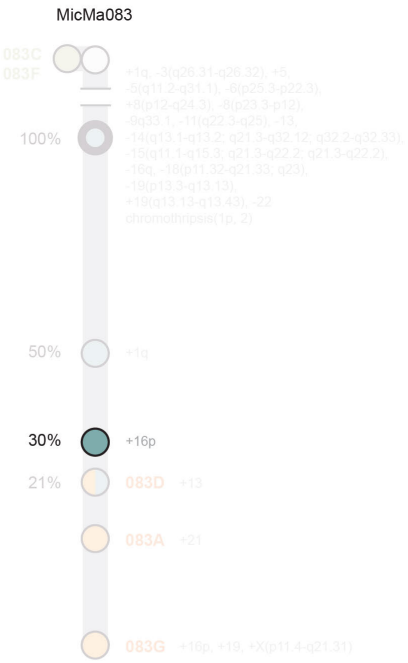
D

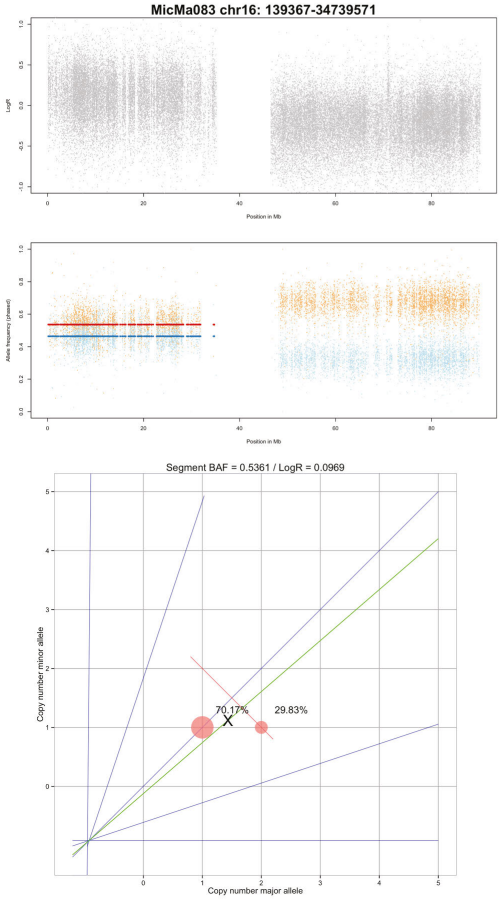

MicMa083
083C
083F
+1q, -3(q26.31-q26.32), +5,
-5(q11.2-q31.1), -6(p25.3-p22.3),
+8(p12-q24.3), -8(p23.3-p12),
-9(q33.1 -11(q22.3-q25), -13,
100%
-14(q13.1-q13.2; q21.3-q32.12; q32.2-q32.33),
-15(q11.1-q15.3; q21.3-q22.2- q21.3-q22.2),
-16q, -18(p11.32-q21.33; q23),
-19(p13.3-q13.13),
+19(q13.13-q13.43), -22
chromothripsis(1p, 2)
50%
+1q
30%
+16p
21%
083D
+13
083A
+21
083G
+16p, +19, +X(p11.4-q21.31)


MicMa083 chr1: 145394955-249190891
LogR
Position in Mb
Allele frequency (phased)
Position in Mb


Segment BAF = 0.6407 / LogR = 0.2819
Copy number minor allele
49.78%
50.22%
Copy number major allele

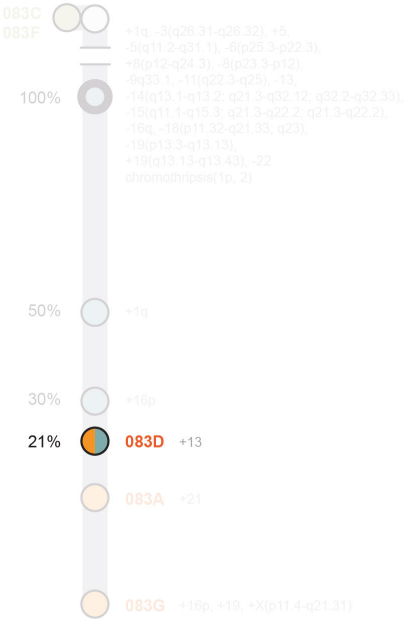
E

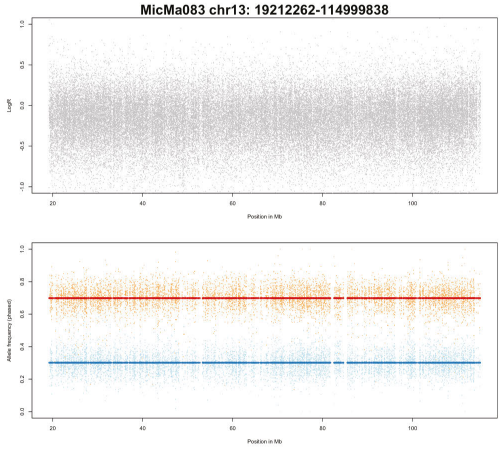

MicMa083
083C
083F
+1q, -3(q26.31-q26.32), +5,
-5(q11.2-q31.1), -6(p25.3-p22.3),
+8(p12-q24.3), -8(p23.3-p12),
-9q33.1, -11(q22.3-q25), -13,
100%
-14(q13.1-q13.2; q21.3-q32.12; q32.2-q32.33),
-15(q11.1-q15.3; q21.3-q22.2; q21.3-q22.2),
-16q, -18(p11.32-q21.33; q23),
-19(p13.3-q13.13),
+19(q13.13-q13.43), -22
chromothripsis(1p; 2)
50%
+1q
30%
+16p
21%
083D
+13
083A
+21
083G
+16p, +19, +X(p11.4-q21.31)

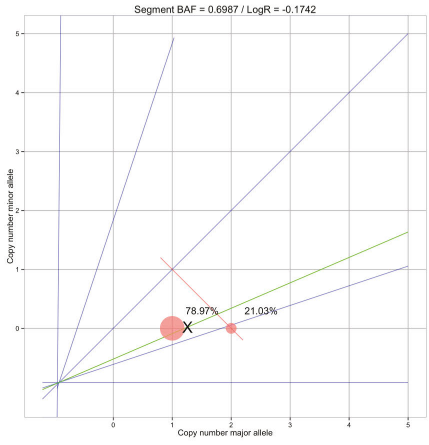

MicMa083 chr16: 139367-34739571
LogR
Position in Mb
Allele frequency (phased)
Position in Mb
Segment BAF = 0.5361 / LogR = 0.0969
Copy number minor allele
70.17%
29.83%
Copy number major allele

F

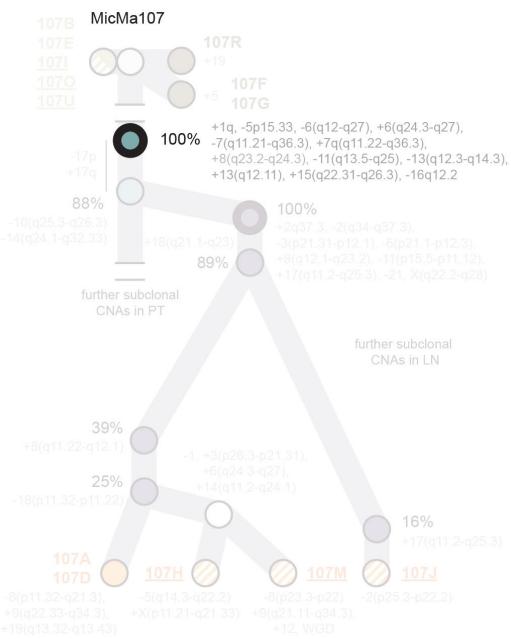
MicMa083

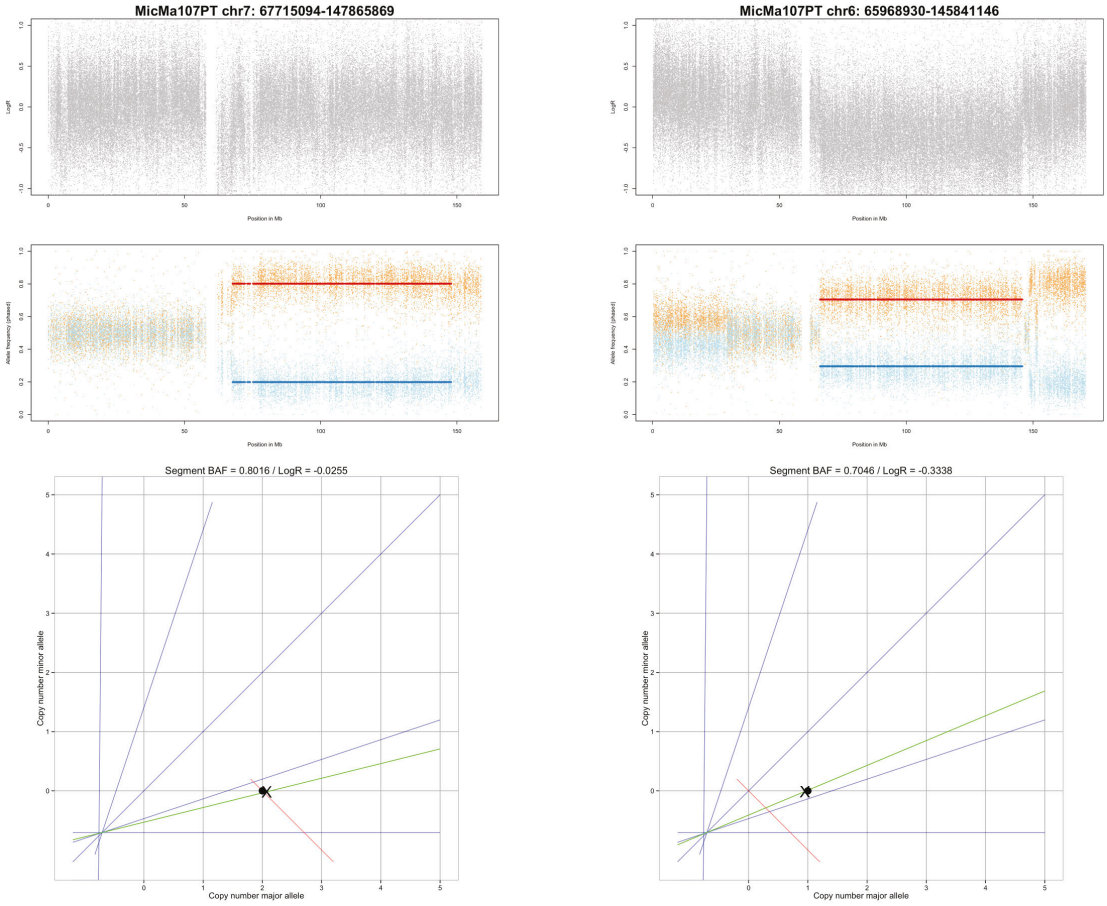

083C
083F
+1q, -3(q26.31-q26.32), +5,
-5(q11.2-q31.1), -6(p25.3-p22.3),
+8(p12-q24.3), -8(p23.3-p12),
-9q33.1, -11(q22.3-q25), -13,
100%
-14(q13.1-q13.2, q21.3-q32.12; q32.2-q32.33),
-15(q11.1-q15.3; q21.3-q22.2; q21.3-q22.2),
-16q, -18(p11.32-q21.33; q23),
-19(p13.3-q13.13),
+19(q13.13-q13.43), -22
chromothripsis(1p, 2)
50%
+1q
30%
+16p
21%
083D
+13
083A
+21
083G
+18p, +19, +X(p11.4-q21.31)


MicMa083 chr13: 19212262-114999838
LogR
Position in Mb
Allele frequency (phased)
Position in Mb

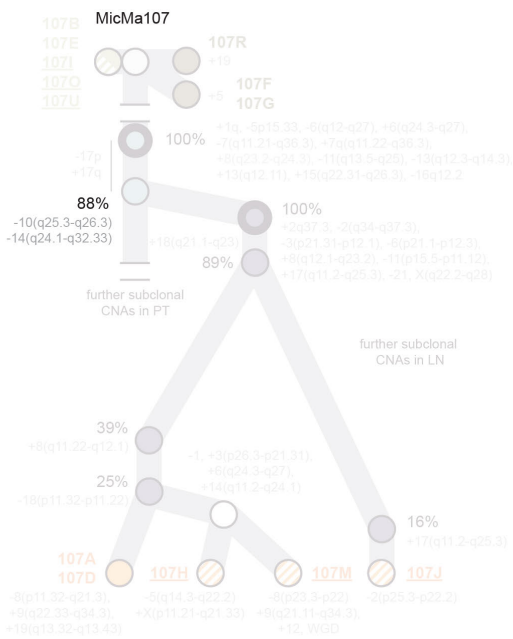

Segment BAF = 0.6987 / LogR = -0.1742
Copy number minor allele
78.97%
21.03%
Copy number major allele

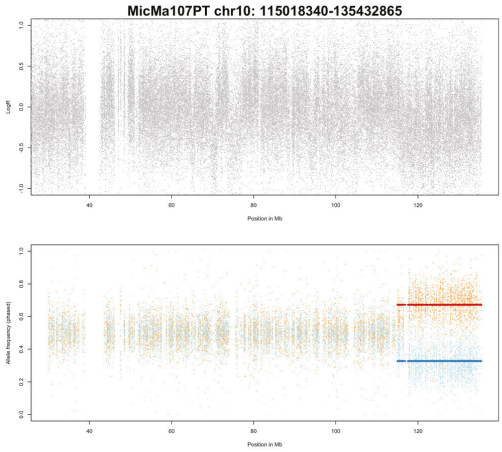
G

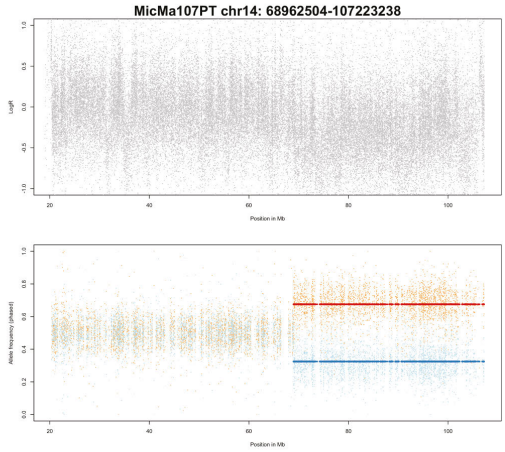

MicMa107
107B
107E
107I
107O
107U
107R
+19
107F
+5
107G
100%
+1q, -5p15.33, -6(q12-q27), +6(q24.3-q27),
-7(q11.21-q36.3), +7q(q11.22-q36.3),
+8(q23.2-q24.3), -11(q13.5-q25), -13(q12.3-q14.3),
+13(q12.11), +15(q22.31-q26.3), -16q12.2
-17p
+17q
88%
-10(q25.3-q26.3)
-14(q24.1-q32.33)
+18(q21.1-q23)
100%
+2(q37.3), -2(q34-q37.3),
-3(p21.31-p12.1), -6(p21.1-p12.3),
+8(q12.1-q23.2), -11(p15.5-p11.12),
+17(q11.2-q25.3), -21, X(q22.2-q28)
89%
further subclonal
CNAs in PT
further subclonal
CNAs in LN
39%
+8(q11.22-q12.1)
-1, +3(p26.3-p21.31),
+6(q24.3-q27),
+14(q11.2-q24.1)
25%
-18(p11.32-p11.22)
16%
+17(q11.2-q25.3)
107A
107D
107H
107M
107J
-8(p11.32-q21.3),
+9(q22.33-q34.3),
+19(q13.32-q13.43)
-5(q14.3-q22.2)
+X(p11.21-q21.33)
-9(p23.3-p22),
+9(q21.11-q34.3),
+12, WGD
-2(p25.3-p22.2)

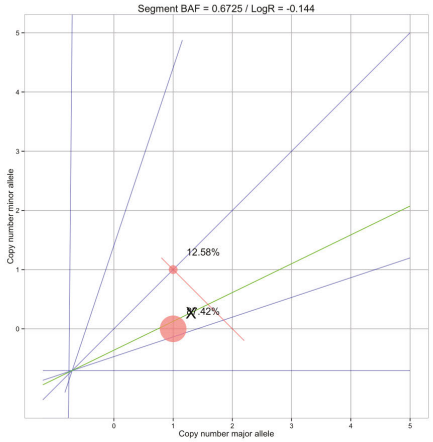

MicMa107PT chr7: 67715094-147865869
MicMa107PT chr6: 65968930-145841146
LogR
Allele frequency (observed)
Position in Mb
Segment BAF = 0.8016 / LogR = -0.0255
Segment BAF = 0.7046 / LogR = -0.3338
Copy number minor allele
Copy number major allele

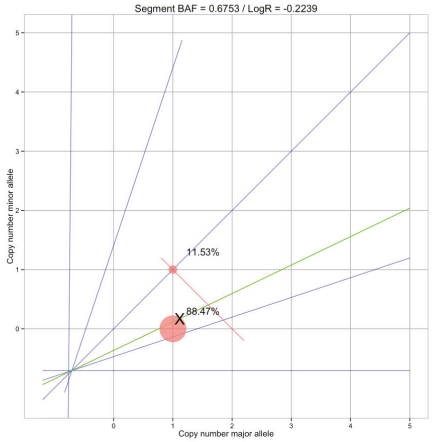
H

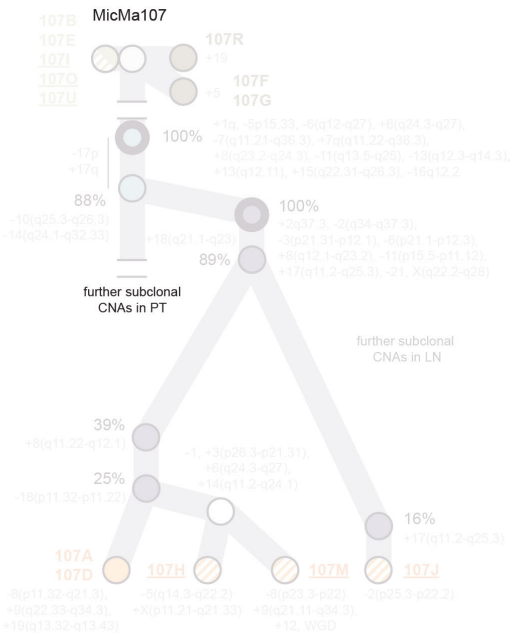

MicMa107
107B
107E
107I
107O
107U
107R
+19
107F
107G
+5
100%
+1q, -5p15.33, -6(q12-q27), +6(q24.3-q27),
-7(q11.21-q36.3), +7q(q11.22-q36.3),
+8(q23.2-q24.3), -11(q13.5-q25), -13(q12.3-q14.3),
+13(q12.11), +15(q22.31-q26.3), -16q12.2
-17p
+17q
88%
-10(q25.3-q26.3)
-14(q24.1-q32.33)
+18(q21.1-q23)
100%
+2q37.3, -2(q34-q37.3),
-3(p21.31-p12.1), -6(p21.1-p12.3),
+8(q12.1-q23.2), -11(p15.5-p11.12),
+17(q11.2-q25.3), -21, X(q22.2-q28)
89%
further subclonal
CNAs in PT
further subclonal
CNAs in LN
39%
+8(q11.22-q12.1)
-1, +3(p26.3-p21.31),
+6(q24.3-q27),
+14(q11.2-q24.1)
25%
-18(p11.32-p11.22)
16%
+17(q11.2-q25.3)
107A
107D
107H
107M
107J
-8(p11.32-q21.3),
+9(q22.33-q34.3),
+19(q13.32-q13.43)
-5(q14.3-q22.2)
+X(p11.21-q21.33)
-9(p23.3-p22),
+9(q21.11-q34.3),
+12, WGD
-2(p25.3-p22.2)

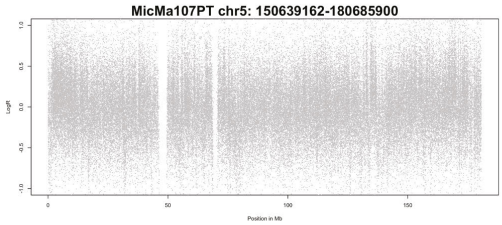

MicMa107PT chr10: 115018340-135432865
LogR
Position in Mb
Allele frequency (phased)

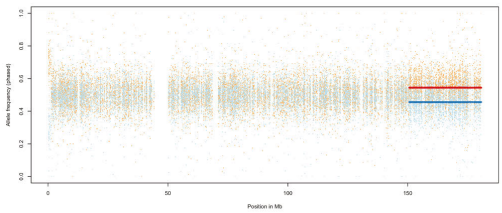

MicMa107PT chr14: 68962504-107223238
LogR
Position in Mb
Allele frequency (phased)

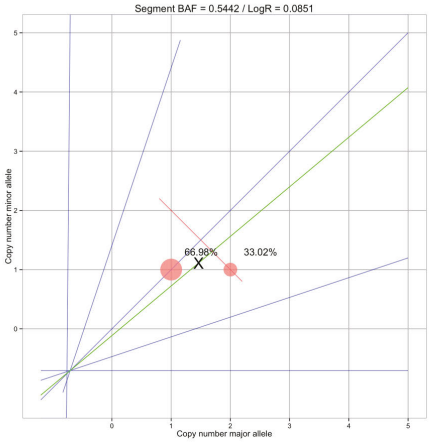

Segment BAF = 0.6725 / LogR = -0.144
12.58%
87.42%
Copy number minor allele
Copy number major allele

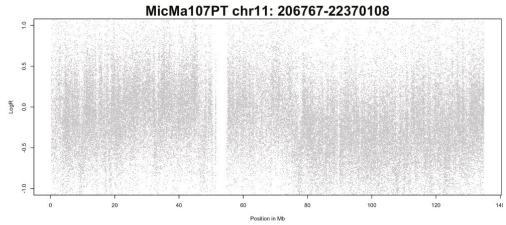

Segment BAF = 0.6753 / LogR = -0.2239
11.53%
88.47%
Copy number minor allele
Copy number major allele

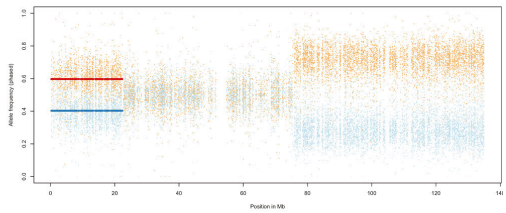

MicMa107
107B
107E
107I
107O
107U
107R
+19
107F
107G
+5
100%
+1q, -5p15.33, -6(q12-q27), +6(q24.3-q27),
-7(q11.21-q36.3), +7q(q11.22-q36.3),
+8(q23.2-q24.3), -11(q13.5-q25), -13(q12.3-q14.3),
+13(q12.11), +15(q22.31-q26.3), -16q12.2
-17p
+17q
88%
-10(q25.3-q26.3)
-14(q24.1-q32.33)
+18(q21.1-q23)
100%
+2q37.3, -2(q34-q37.3),
-3(p21.31-p12.1), -6(p21.1-p12.3),
+8(q12.1-q23.2), -11(p15.5-p11.12),
+17(q11.2-q25.3), -21, X(q22.2-q28)
89%
further subclonal
CNAs in PT
further subclonal
CNAs in LN
39%
+8(q11.22-q12.1)
-1, +3(p26.3-p21.31),
+6(q24.3-q27),
+14(q11.2-q24.1)
25%
-18(p11.32-p11.22)
16%
+17(q11.2-q25.3)
107A
107D
107H
107M
107J
-8(p11.32-q21.3),
+9(q22.33-q34.3),
+19(q13.32-q13.43)
-5(q14.3-q22.2)
+X(p11.21-q21.33)
-9(p23.3-p22),
+9(q21.11-q34.3),
+12, WGD
-2(p25.3-p22.2)

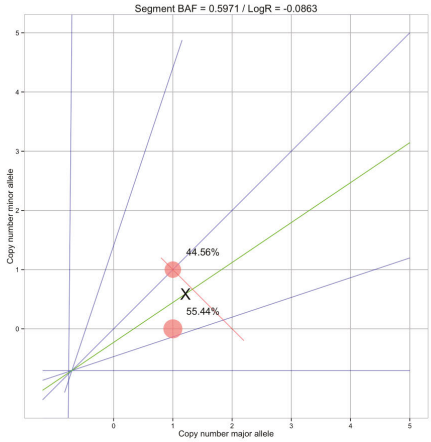

MicMa107PT chr5: 150639162-180685900
LogR
Position in Mb


Allele frequency (observed)
Position in Mb

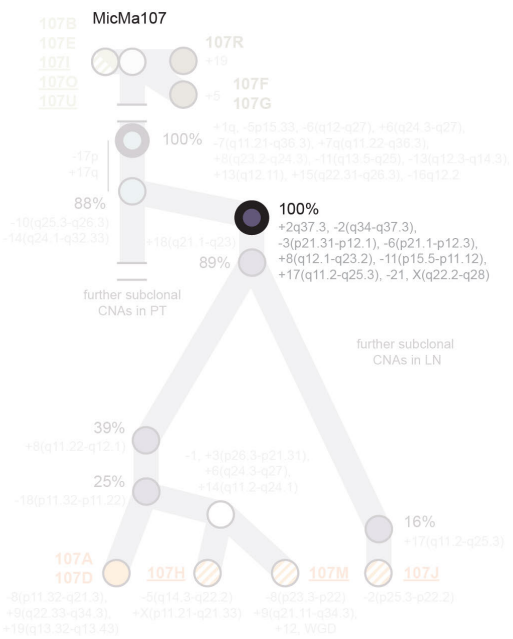

Segment BAF = 0.5442 / LogR = 0.0851
66.98%
33.02%
Copy number minor allele
Copy number major allele

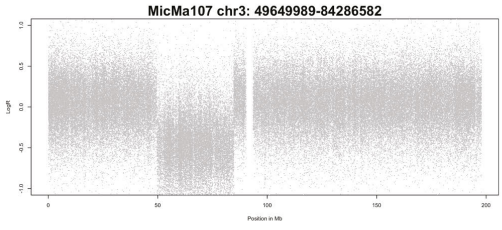

MicMa107PT chr11: 206767-22370108
LogR
Position in Mb

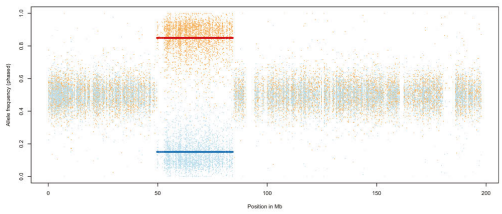

Allele frequency (observed)
Position in Mb

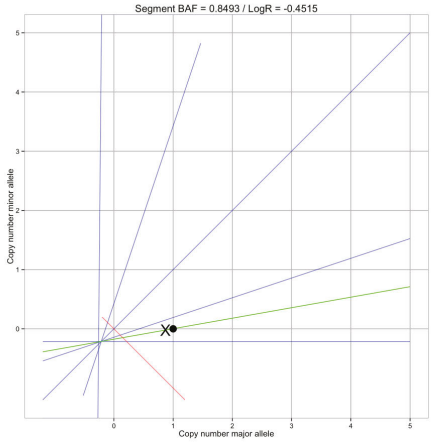

Segment BAF = 0.5971 / LogR = -0.0863
44.56%
55.44%
Copy number minor allele
Copy number major allele

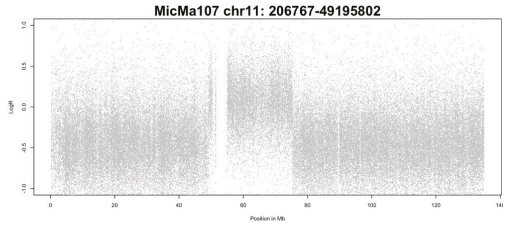
J

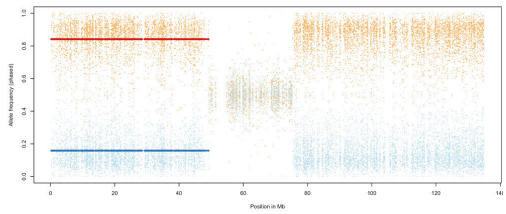

MicMa107
107B
107E
107I
107O
107U
107R
+19
107F
107G
+5
100%
+1q, -5p15.33, -6(q12-q27), +6(q24.3-q27),
-7(q11.21-q36.3), +7q(q11.22-q36.3),
+8(q23.2-q24.3), -11(q13.5-q25), -13(q12.3-q14.3),
+13(q12.11), +15(q22.31-q26.3), -16q12.2
-17p
+17q
88%
-10(q25.3-q26.3)
-14(q24.1-q32.33)
+18(q21.1-q23)
100%
+2q37.3, -2(q34-q37.3),
-3(p21.31-p12.1), -6(p21.1-p12.3),
+8(q12.1-q23.2), -11(p15.5-p11.12),
+17(q11.2-q25.3), -21, X(q22.2-q28)
89%
further subclonal
CNAs in PT
further subclonal
CNAs in LN
39%
+8(q11.22-q12.1)
-1, +3(p26.3-p21.31),
+6(q24.3-q27),
+14(q11.2-q24.1)
25%
-18(p11.32-p11.22)
16%
+17(q11.2-q25.3)
107A
107D
107H
107M
107J
-8(p11.32-q21.3),
+9(q22.33-q34.3),
+19(q13.32-q13.43)
-5(q14.3-q22.2)
+X(p11.21-q21.33)
-9(p23.3-p22)
+9(q21.11-q34.3),
+12, WGD
-2(p25.3-p22.2)

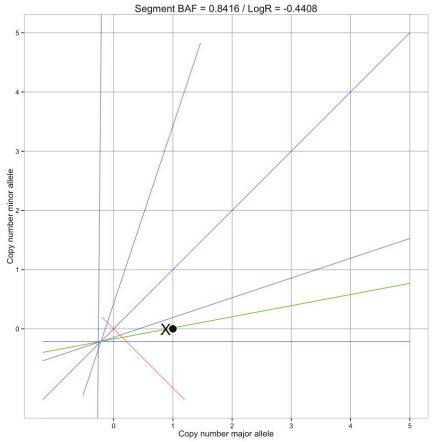

MicMa107 chr3: 49649989-84286582
LogR
Position in Mb


Allele frequency (phased)
Position in Mb

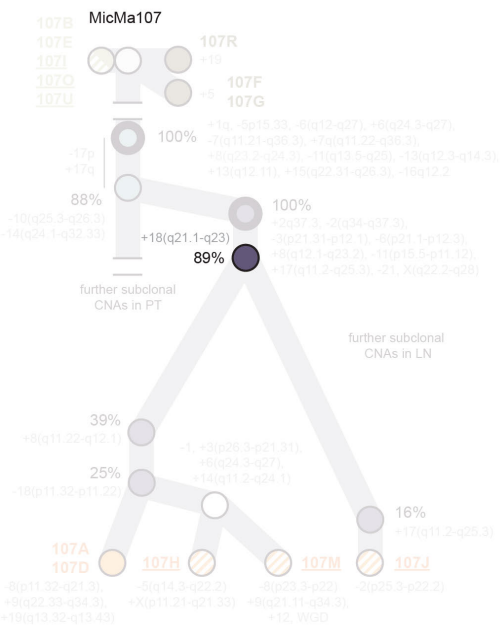

Segment BAF = 0.8493 / LogR = -0.4515
Copy number minor allele
Copy number major allele

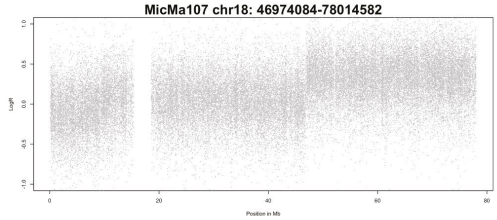

MicMa107 chr11: 206767-49195802
LogR
Position in Mb

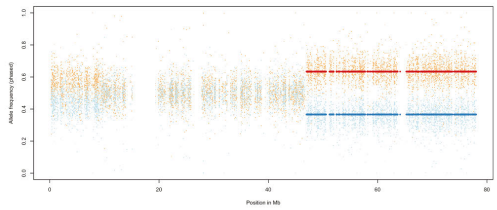

Allele frequency (phased)
Position in Mb

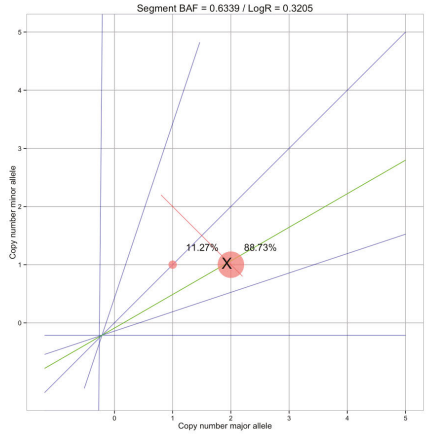

Segment BAF = 0.8416 / LogR = -0.4408
Copy number minor allele
Copy number major allele

K

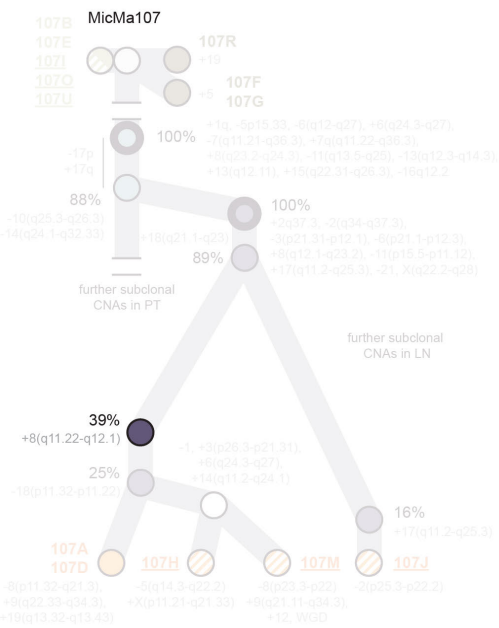

MicMa107
107B
107E
107I
107O
107U
107R
+19
107F
107G
+5
100%
+1q, -5p15.33, -6(q12-q27), +6(q24.3-q27),
-7(q11.21-q36.3), +7q(q11.22-q36.3),
+8(q23.2-q24.3), -11(q13.5-q25), -13(q12.3-q14.3),
+13(q12.11), +15(q22.31-q26.3), -16q12.2
-17p
+17q
88%
-10(q25.3-q26.3),
-14(q24.1-q32.33)
100%
+2q37.3, -2(q34-q37.3),
-3(p21.31-p12.1), -6(p21.1-p12.3),
+8(q12.1-q23.2), -11(p15.5-p11.12),
+17(q11.2-q25.3), -21, X(q22.2-q28)
+18(q21.1-q23)
89%
further subclonal
CNAs in PT
further subclonal
CNAs in LN
39%
+8(q11.22-q12.1)
25%
-18(p11.32-p11.22)
-1, +3(p26.3-p21.31),
+6(q24.3-q27),
+14(q11.2-q24.1)
16%
+17(q11.2-q25.3)
107A
107D
107H
107M
107J
-8(p11.32-q21.3),
+9(q22.33-q34.3),
+19(q13.32-q13.43)
-5(q14.3-q22.2)
+X(p11.21-q21.33)
-9(p23.3-p22)
+8(q21.11-q34.3),
+12, WGD
-2(p25.3-p22.2)

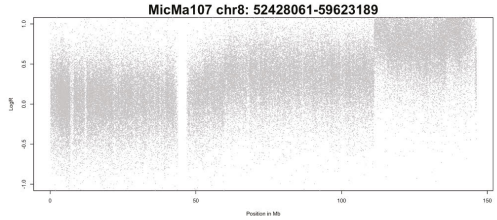

MicMa107 chr18: 46974084-78014582
LogR
Position in Mb

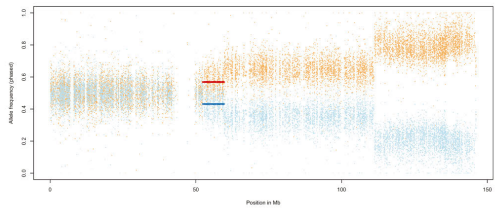

Allele frequency (phased)
Position in Mb

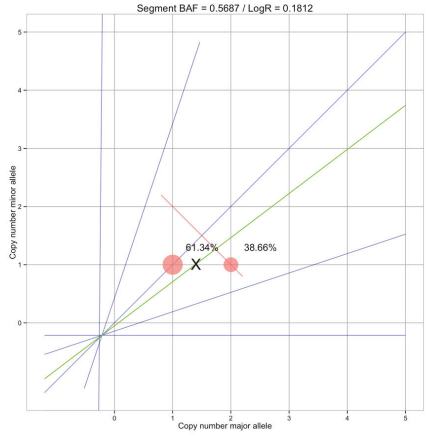

Segment BAF = 0.6339 / LogR = 0.3205
11.27%
88.73%
X
Copy number minor allele
Copy number major allele

L

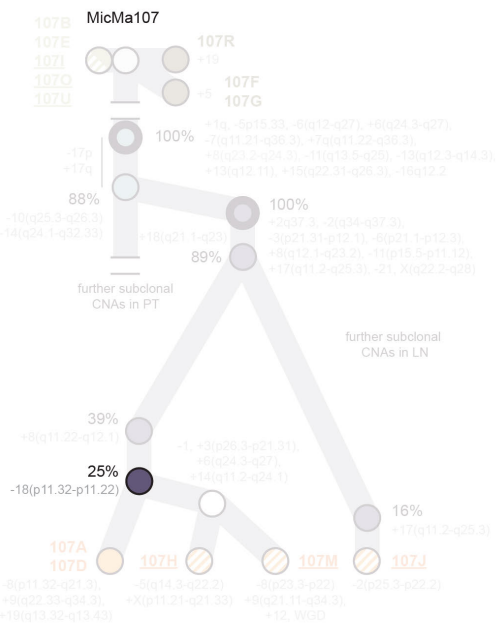

MicMa107
107B
107E
107I
107O
107U
107R
+19
107F
107G
+5
100%
+1q, -5p15.33, -6(q12-q27), +6(q24.3-q27),
-7(q11.21-q36.3), +7q(q11.22-q36.3),
+8(q23.2-q24.3), -11(q13.5-q25), -13(q12.3-q14.3),
+13(q12.11), +15(q22.31-q26.3), -16q12.2
-17p
+17q
88%
-10(q25.3-q26.3),
-14(q24.1-q32.33)
+18(q21.1-q23)
100%
+2q37.3, -2(q34-q37.3),
-3(p21.31-p12.1), -6(p21.1-p12.3),
+8(q12.1-q23.2), -11(p15.5-p11.12),
+17(q11.2-q25.3), -21, X(q22.2-q28)
89%
further subclonal
CNAs in PT
further subclonal
CNAs in LN
39%
+8(q11.22-q12.1)
-1, +3(p26.3-p21.31),
+6(q24.3-q27),
+14(q11.2-q24.1)
25%
-18(p11.32-p11.22)
16%
+17(q11.2-q25.3)
107A
107D
107H
107M
107J
-8(p11.32-q21.3),
+9(q22.33-q34.3),
+19(q13.32-q13.43)
-5(q14.3-q22.2)
+X(p11.21-q21.33)
-9(p23.3-p22)
+8(q21.11-q34.3),
+12, WGD
-2(p25.3-p22.2)

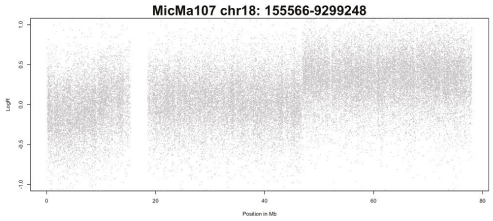

MicMa107 chr8: 52428061-59623189
LogR
Position in Mb

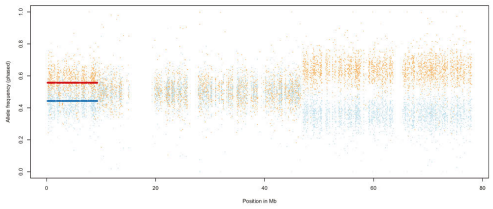

Allele frequency (phased)
Position in Mb

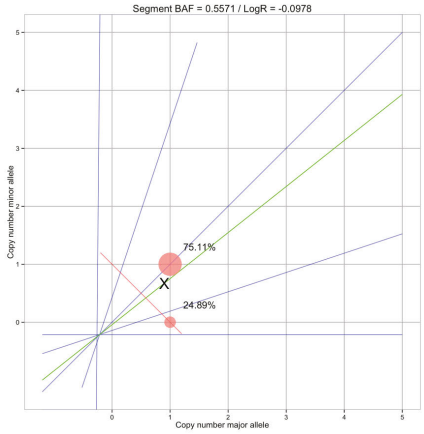

Segment BAF = 0.5687 / LogR = 0.1812
61.34%
38.66%
Copy number minor allele
Copy number major allele

M

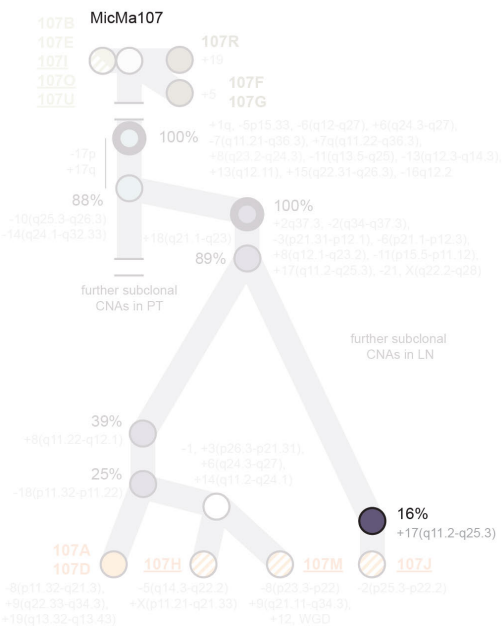

MicMa107
107B
107E
107I
107O
107U
107R
+19
107F
107G
-5
100%
+1q, -5p15.33, -6(q12-q27), +8(q24.3-q27),
-7(q11.21-q36.3), +7q(q11.22-q36.3),
+8(q23.2-q24.3), -11(q13.5-q25), -13(q12.3-q14.3),
+13(q12.11), +15(q22.31-q26.3), -16q12.2
-17p
+17q
88%
-10(q25.3-q26.3),
-14(q24.1-q32.33)
+18(q21.1-q23)
100%
+2q(q37.3, -2(q34-q37.3),
-3(p21.31-p12.1), -6(p21.1-p12.3),
+8(q12.1-q23.2), -11(p15.5-p11.12),
+17(q11.2-q25.3), -21, X(q22.2-q28)
89%
further subclonal
CNAs in PT
further subclonal
CNAs in LN
39%
+8(q11.22-q12.1)
-1, +3(p26.3-p21.31),
+6(q24.3-q27),
+14(q11.2-q24.1)
25%
-18(p11.32-p11.22)
16%
+17(q11.2-q25.3)
107A
107D
107H
107M
107J
8(p11.32-q21.3),
+9(q22.33-q34.3),
+19(q13.32-q13.43)
-5(q14.3-q22.2),
+X(p11.21-q21.33)
-8(p23.3-p22),
+9(q21.11-q34.3),
+12, WGD
2(p25.3-p22.2)

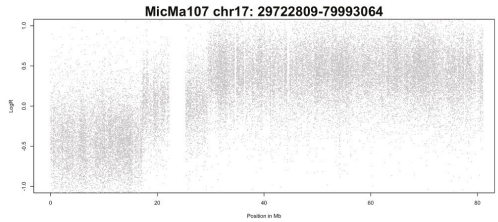

MicMa107 chr18: 155566-9299248
LogR
Position in Mb

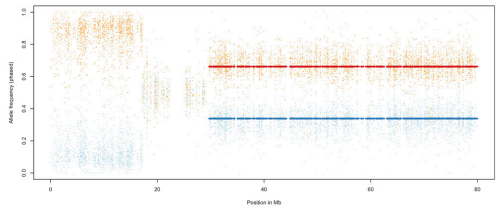

Allele frequency (phased)
Position in Mb

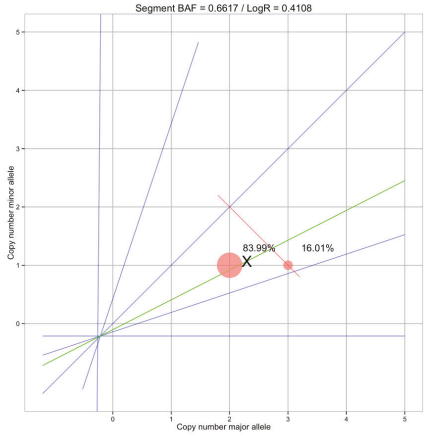

Segment BAF = 0.5571 / LogR = -0.0978
Copy number minor allele
Copy number major allele
75.11%
24.89%
X

N

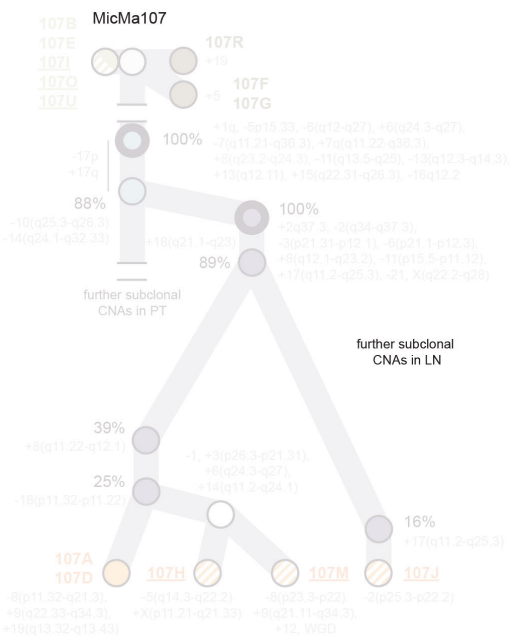

MicMa107
107B
107E
107I
107O
107U
107R
+19
107F
107G
+5
100%
+1q, -5p15.33, -6(q12-q27), +6(q24.3-q27),
-7(q11.21-q36.3), +7q(q11.22-q36.3),
+8(q23.2-q24.3), -11(q13.5-q25), -13(q12.3-q14.3),
+13(q12.11), +15(q22.31-q26.3), -18q12.2
-17p
+17q
88%
-10(q25.3-q26.3),
-14(q24.1-q32.33)
100%
+2q37.3, -2(q34-q37.3),
-3(p21.31-p12.1), -6(p21.1-p12.3),
+8(q12.1-q23.2), -11(p15.5-p11.12),
+17(q11.2-q25.3), -21, X(q22.2-q28)
+18(q21.1-q23)
89%
further subclonal
CNAs in PT
further subclonal
CNAs in LN
39%
+8(q11.22-q12.1)
-1, +3(p26.3-p21.31),
+6(q24.3-q27),
+14(q11.2-q24.1)
25%
-18(p11.32-p11.22)
16%
+17(q11.2-q25.3)
107A
107D
107H
107M
107J
-8(p11.32-q21.3),
+9(q22.33-q34.3),
+19(q13.32-q13.43)
-5(q14.3-q22.2)
+X(p11.21-q21.33)
-8(p23.3-p22)
+9(q21.11-q34.3),
+12, WGD
-2(p25.3-p22.2)

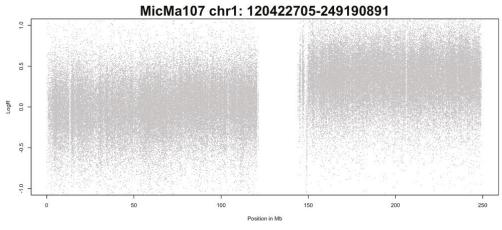

MicMa107 chr17: 29722809-79993064
LogR
Position in Mb

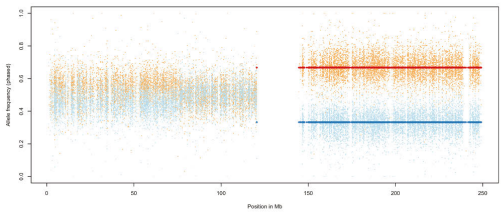

Allele frequency (observed)
Position in Mb

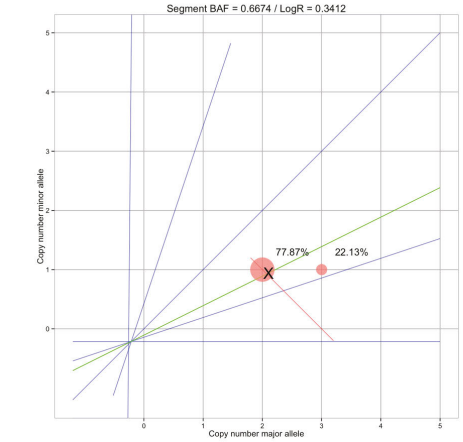

Segment BAF = 0.6617 / LogR = 0.4108
83.99%
16.01%
Copy number minor allele
Copy number major allele

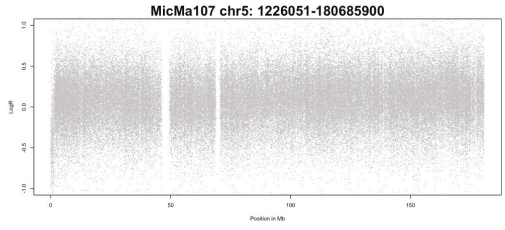
O

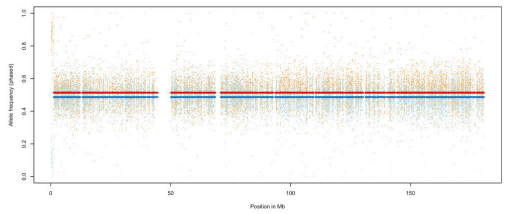

MicMa107
107B
107E
107I
107O
107U
107R
+19
107F
+5
107G
100%
+1q, -5p15.33, -6(q12-q27), +6(q24.3-q27),
-7(q11.21-q36.3), +7q(q11.22-q36.3),
+8(q23.2-q24.3), -11(q13.5-q25), -13(q12.3-q14.3),
+13(q12.11), +15(q22.31-q26.3), -16q12.2
-17p
+17q
88%
-10(q25.3-q26.3)
-14(q24.1-q32.33)
+18(q21.1-q23)
100%
+2q37.3, -2(q34-q37.3),
-3(p21.31-p12.1), -6(p21.1-p12.3),
+8(q12.1-q23.2), -11(p15.5-p11.12),
+17(q11.2-q25.3), -21, X(q22.2-q28)
89%
further subclonal
CNAs in PT
further subclonal
CNAs in LN
39%
+8(q11.22-q12.1)
-1, +3(p26.3-p21.31),
+6(q24.3-q27),
+14(q11.2-q24.1)
25%
-18(p11.32-p11.22)
16%
+17(q11.2-q25.3)
107A
107D
107H
107M
107J
-8(p11.32-q21.3),
+9(q22.33-q34.3),
+19(q13.32-q13.43)
-5(q14.3-q22.2)
+X(p11.21-q21.33)
-9(p23.3-p22),
+9(q21.11-q34.3),
+12, WGD
-2(p25.3-p22.2)


MicMa107 chr1: 120422705-249190891
LogR
Position in Mb


Allele frequency (observed)
Position in Mb


Segment BAF = 0.6674 / LogR = 0.3412
77.87%
22.13%
Copy number minor allele
Copy number major allele


MicMa107 chr5: 1226051-180685900
LogR
Position in Mb


Allele frequency (observed)
Position in Mb

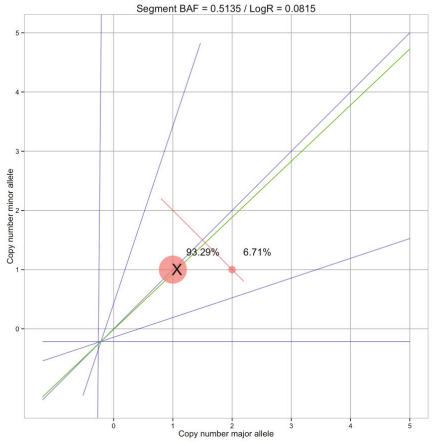

Segment BAF = 0.5135 / LogR = 0.0815
93.29%
6.71%
Copy number minor allele
Copy number major allele

Figure S10: Flowchart of bulk exome sequence analysis. The steps schematically outline our workflow to detect somatic mutations in the bulk tumor exomes and filter out putative false positives.